Vitiligo: Clinical Associations and Trend in South East Nigeria.

E. N. Nnoruka *Msc.Clin. Derm. (Lond.), FMCP(Nig.)*
Sub-Dept of Dermatology, College of Medicine, UNTH, Enugu, Nigeria.
Correspondence to: Dr. E.N. Nnoruka, Sub-Department of Dermatology, College of Medicine, University of Nigeria Teaching Hospital, Enugu, Nigeria. E-mail: nkechi_nnoruka@yahoo.com

Background: **Vitiligo is a cosmetically disfiguring disease, of which the psychological impact can be of paramount importance in deeply pigmented races, particularly Africans. This sharp contrast usually carries severe social stigma. The natural course of the disease is unpredictable, and several studies have dealt with epidemiological features, prevalence, familial aggregation, sex, age distribution, clinical presentation and associations, which have been reported mainly from white populations. Not many of such studies have been performed in African blacks, to show the clinical associations and disease trends observed in the region.**

Aim: **To document the trends, associations, percentage of body surface involvement, status of disease activity, and response to treatment options offered; as seen in South East Nigeria, West Africa.**

***Methodology*:** **A prospective study of 751 consecutive vitiligo patients was carried out at the Dermatology clinic of the University of Nigeria Teaching Hospital over a two-year period. Diagnosis was accomplished by direct clinical examination, followed by examination of the depigmented areas under Wood's light. Full blood count, random blood sugar/ fasting blood sugar levels, thyroid function tests and investigations for common circulating autoantibodies such as ANA (anti-nuclear antibodies) and lupus erythematosus cell (LE) test, were carried out to rule out any associations with vitiligo. Skin biopsies were carried out for standard pathologic examination to help confirm the diagnosis in 11 cases. A control group of 350 normal patients without vitiligo were selected from patients attending the general outpatient department of the same teaching hospital.**

Results: **The incidence of vitiligo was 5.8%. Family history of vitiligo was present in 17 (2.3%). Fifteen (1.9%) suffered from diabetes mellitus, 9 (1.2%) thyroid disease, 10(1.3%) atopic dermatitis, 3 (0.4%) sarcoidosis, while 7(1%) had lepramatous leprosy. Kobners phenomenon was observed in 57.3% (430 patients). Sixty- seven percent of the lesions were on exposed areas. It was purely acral in 47(6.3%), acrofacial in161 (21.5%), segmental in 50 (6.6%), pure mucosal in 13 (1.7%) and generalized in 20(2.6%). The extent of involvement was 1% or less in 180(32.8%) and 75% and above in 9(1.2%) patients. The disease progression was continuously slow in 411(54.7%), slow with periods of rapid exacerbation in 138(18.4%), rapid in 67 (8.9%), and in 59(7.9%) patients the disease had been static for more than 6 months within the study period. Koebner's phenomenon, a family history of vitiligo and mucous membrane involvement showed more progression of vitiligo. Trigger factors also recorded included cosmetics, concoctions, rubber, pregnancy and psychological stress only in a few.**

Conclusions: **The pattern of vitiligo observed in our environment is similar to that reported elsewhere. Clinical characteristics such as family history, clinical type, duration of disease, Koebner's phenomenon, and mucous membrane involvement, were relevant in predicting the progression/ prognosis of vitiligo in South Eastern Nigeria.**

***Key Words*:** **Vitiligo, associations, treatment, Nigeria**

INTRODUCTION

Vitiligo is a common acquired idiopathic skin disorder characterized by one or more patches of depigmentation caused by loss of cutaneous melanocytes. It is associated with a lot of emotional exhaustion, cosmetic disfiguration and psychological disturbances. The disease affects 0.5%-4% of the population[1, 2] involving all races and ethnic groups.

The natural course of vitiligo is uncertain and difficult to predict in patients. Given the stark contrast between depigmented areas and darker skin tones, vitiligo is most cosmetically disfiguring for darker races and ethnic groups with resultant social and economic disadvantage. It is a frequent reason for consultation at our dermatology clinic in South Eastern Nigeria.

Vitiligo is often classified into three types, generalized, segmental, and localized, on the basis of their distribution pattern. It may also classified into type A (non-dermatomal or non-segmental) and type B (dermatomal or segmental) vitiligo on the basis of both the distribution pattern and physiological function [3,4]. The natural courses of type A and type B vitiligo are characteristic and quite different from each other. Whereas type A vitiligo appears at any age and progresses throughout the patient's life span, type B vitiligo affects the young and stabilizes within a few years. Segmental type vitiligo corresponds to type B, and generalized type vitiligo is the late stage of type A. However certain clinical aspects may suggest some trends in a patient, based on which the treatment modalities may be selected or avoidable triggers may be identified.

A prospective study was therefore conducted on patients with vitiligo to evaluate the clinical features of vitiligo in South East Nigeria. The main objective was to assess the clinical features such as age of onset, extent of involvement, type of distribution of lesions, percentage of body surface involvement, trigger factors; associated phenomenon and status of the disease in terms of disease progression as well as response to treatment offered.

METHODOLOGY:

A prospective study was carried out between February 1999 and January 2001, 13,045 outpatients were seen at the Skin clinic of the University of Nigeria teaching Hospital. Of these, 751 consecutive patients with vitiligo were involved with this study and followed up for the study period. Their ages ranged from 3 to 77 years. They were questioned about their disease which included family history, age, duration of their disease, circumstances of their vitiligo onset and if there was any other associated symptoms such as polyuria, polydypsia and polyphagia. The following were recorded based on the history and clinical findings; age of onset, sex, site of initial lesion, evidence of trigger factor, associated phenomenon /disease, status of disease activity and percentage of body surface involved. The same dermatologist, the author to ensure the diagnosis, examined patients. Diagnosis was accomplished by direct clinical examination, followed by examination of the depigmented areas under Wood's light. Skin biopsies were carried out for standard pathologic examination and were carried out in 11 cases, to confirm diagnosis. The following tests were also carried out to rule out any associations between vitiligo and other disorders/autoimmune diseases. These tests included full blood count and its differentials, random blood sugar/ fasting blood sugar levels, thyroid function tests and investigations for common circulating autoantibodies such as ANA (anti-nuclear antibodies), thyroid autoantibodies and lupus erythematosus cell (LE) test, based on the facilities available. A control group of 350 normal patients were selected from patients attending the general outpatient department of the same teaching hospital. After giving informed consent all potential control subjects were examined to select persons free of vitiligo and to detect the presence of other skin diseases.

Statistical Analysis

All analysis were performed using the Statistical Programme for Social Sciences (SPSS) package, with a 95% confidence level. The prevalence of clinical and laboratory characteristics in patients were reported as percentages.

RESULTS:

Of the 13,045 patients examined, vitiligo was detected in 751(478 females and 273 males; sex ratio 0.6). The incidence of vitiligo at the University of Nigeria Teaching Hospital, Enugu Nigeria was 5.8% for the period from 1999- 2001. The age of onset of the disease was less than 5 years in 8.7%, 5-15 years in 39.7%, 16-40 years in 35.6%, 41- 60years in 14. 5% and ≥ 60 years in 2.7%. The mean age for onset of the disease was 28.3 and females were the most affected (tables I and II).

Table I. Sex Distribution of patients with Vitiligo and Controls.

Number of patients involved with the study			
	Male	Female	Total
Vitiligo	273 (36.4%)	478 (63.6%)	751
Without Vitiligo (Control)	134 (38.2%)	216(61.8%)	350

TABLE II: Clinical Characteristics of Patients with Vitiligo and their Control.

Variable	Vitiligo (n=751)	Control (n=350)	pVal
Mean age (yrs)	28.25	27.13	0.506
Sex (%)			
Female	63.6%	61.8%	0.799
Male	36.4%	38.2%	0.693
Family history of vitiligo (%)	2.3%	0.3%	0.00001
History of autoimmune disease (%)	8.1%	1.2%	0.001
Koebners phenomenon (%)	57.3%	1.4%	0.000001

Family history of vitiligo / premature graying was present in 17 (2.3%) cases, while one patient had three out of five sibs affected with vitiligo; only 1 control (0.3%) had a family history of vitiligo. Fifteen (1.9%) suffered from diabetes mellitus while two (0.6 %)of the controls had diabetes melitus, 9(1.2%) patients and one control (0.3%) had thyroid disease, 10(1.3%) had atopic dermatitis, 3 (0.4%) had sarcoidosis, while 7(1%) had lepramatous leprosy (table III). None of the controls had atopic dermatitis, alopecia areata, sarcoidosis nor leprosy. Family history of vitiligo was significantly more amongst patients with vitiligo than their control ($p \leq 0.000001$). Similarly, Koebner's phenomenon, history of autoimmune disease in the patient, and history of vitiligo, were all significantly more amongst cases than the controls. Table II reflects the clinical characteristics of patients with vitiligo and their control.

Poliosis was present in 298 patients (39.7%). The eyebrows were the most commonly involved (147 patients, 19.6%). In men the involved sites were scalp hair (11.4%), eyebrows (17.2%), and pubic hair (2.3%), whereas in women the eyebrows (24.0%), scalp hair (14.9%) and pubic hair (2.0%)

were involved. Both scalp hair and eyebrows were involved in 69 patients (9.2%).

TABLE III: Associated Diseases Observed Amongst Patients with Vitiligo (n=751)

Disease	No of patients (%)
Atopic Dermatitis	10 (1.3%)
Alopecia Areata	4 (0.5%)
Diabetes Mellitus	15 (2.0%)
Hansen's Disease	7 (1%)
Thyroid Disease	9 (1.2%)
Sarcodosis	3 (0.4%)
Total	48 (6.4%)

Autoimmune vitiligo was suspected in 300 (40%) of cases based on the following criteria; multiple lesions in non-segmental distribution, widespread distribution, rapid progression and extensive disease. 177 of these were investigated for common autoantibodies. ANA (antinuclear antibodies) were detected in 8.1%, anti-thyroglobulin in 23.6% and anti-microsomal antibodies in 31.6% of these 177 cases respectively.

Kobners phenomenon was observed in 57.3%cases (430 patients) while kobnerisation in the controls was observed in 1.4% (4 controls). The age range of patients with koebners phenomenon was from 4-67 years; with a median age of 29years and evidence of trauma as a trigger factor was more prevalent in younger age group.

TABLE IV: Extent of Disease Involvement (n=751)

Body Percentage involvement	No of patients	(%) percentage
≤ 1%	180	32%
1- 10%	364	48.5%
11- 25%	112	14.9%
26- 50%	69	9.2%
51- 75%	17	2.3%
≥ 75%	9	1.2%

Sixty- seven percent of the lesions were in exposed areas. It was purely acral in 47(6.3%), acrofacial in161 (21.5%), vulgaris in 210(27.9%), segmental in 50 (6.6%), pure mucosal in 13 (1.7%) and generalized in 20(2.6%). However 31.7% of the patients also had mucosal involvement in association with other areas affected and 1.9% of the patients had segmental lesions in association with other lesions. The extent of involvement (based on body surface area affected) was 1% or less in 180(32.8%) and 75% and above in 9(1.2%) patients (see table IV). The disease progression was continuously slow in 411(54.7%), slow with periods of rapid exacerbation in 138(18.4%), rapid in 67 (8.9%), and in 59(7.9%) patients the disease had been static for more than 6 months within the study period. Triggers factors recorded include cosmetics (bleaching agents/concoctions) in 9(1.2%), shaving concoction (comprising of methylated spirit, lime and potash) in 3(0.4%), trauma 13(1.7%), pregnancy 4(.5%).

Based on these clinical observations, treatment modalities offered to our patients varied accordingly, however the major non-surgical re-pigmenting therapies were used and included psoralens and corticosteroids; which were used both topically and systemically for well over 70% of the patients. Oral mini pulse therapy with betamethasone or dexamthasone with or without immunosuppressive agents (such as azathioprine or cyclophosphamide) was used for the control of disease activity in the progressive vitiligo cases. For localized disease topical steroids plus sun exposure or topical PUVA plus sun exposure were used; while for slowly progressive vitiligo, levamisole as an immunomodulatory agent used alone or in conjunction with PUVA/PUVA SOL or topical steroid was used.

DISCUSSION:

Vitiligo is a disease of great variation with unpredictable natural course and few data are available regarding the prevalence, associations and trend of vitiligo in black populations for Africans particularly. The incidence of vitiligo from this study was 5.8% similarly as high as an earlier study[5] carried out in the Western part of Nigeria in 1989. Unlike a low prevalence of 0.34% reported from another prevalent study carried out amongst blacks in the French West Indies[6]. The high incidence apart from being a hospital-based study was basically because of the significant disfiguring nature of the disease with its high social and economic impact amongst Nigerian families. It was a frequent cause of outpatient dermatology consultation at the University of Nigeria Teaching Hospital Enugu. Females were affected more from this study in contrast to George[5] who noticed a higher incidence in men in Western Nigeria earlier on. Sex was a biased variable because most of the outpatients at our hospital were females and several studies[7, 8] have shown a preponderance of female patients and vitiligo. This observation is most likely because of the greater likelihood of females to seek medical attention for cosmetic problems.

Vitiligo may develop at any age, but usually begins at 10 to 30 years of age[9, 10].However, according to an epidemiologic study by Howitz et al.[11], approximately 50% of the patients in whom vitiligo developed were older than 40 years of age. From this study the median age for development of vitiligo amongst South Eastern Nigerians was 28.3 years and similarly falls within the commonly observed age range for development of vitiligo amongst other races[9, 10].

In regard to family history of vitiligo, when compared with normal control subjects some significant association was observed. Only 2.3% of our patients had at least one relative with vitiligo unlike previous studies from the Western Part of Nigeria[5] and Libya[12], who reported no family history of vitiligo, amongst the patients they studied. This may probably be due to the fact that in years before now, most African patients were not keen on divulging family histories of such diseases (as vitligo) because of the detrimental social stigma attached to this disorder.

Koebner's phenomenon has been reported in association with vitiligo[13], and its prevalence was high in our patients, with 57.3% and only 1.4% of the controls being affected. These data, alongside a family history of vitiligo, could constitute useful markers of an increased risk for vitiligo, but without association to a specific type of vitiligo. These patients also

exhibited a widespread and rapid progression of their disease. The 5 (1.4%) patients with Koebner's phenomenon in the control group could possibly indicate a vitiligo diathesis, or simply a slowly resolving or permanent hypopigmentation after epidermal trauma in normal subjects.

Vitiligo occurred in seven of our patients with leprosy. These ones had lepromatous leprosy. Over the years, a higher incidence of vitiligo has been observed in our patients with lepromatous leprosy as highlighted by a study on leprosy in our environment, by the author[14]. Both leprosy and vitiligo are known to induce pigment loss via different mech-anisms. Loss of nervous control of melanogenesis could be one of the mechanisms due to nervous damage in leprosy, while for vitiligo the exact mechanisms are unknown [15, 16] However autoimmune disorders have been described in both diseases.

Several authors have emphasized the association of autoimmune diseases with vitiligo[17-18]; we also found a significant association of some autoimmune disease amongst our patients with vitiligo than their controls. In contrast, a family history of these conditions was not significantly observed both amongst our vitiligo patients and their controls.

Despite the fact that autoantibodies were detected amongst some of the 177 patients with vitiligo, these ones did not manifest with any specific autoimmune disorders. This is in keeping with the fact that autoantibodies may be directed against the thyroid and other organ systems without any clinical correlation[19-21]

Poliosis has been associated with vitiligo in 8.9% to 45% of patients[22, 23]. It occurred in 48.6% of our patients. The eyebrows and the scalp hair were most commonly involved (46.7%). Trauma, cosmetics(concotions) psychological stress, pregnancy, and contraceptives may be the precipitating factors of nonsegmental vitiligo. However, unlike other reports[22, 23], it was found that trauma, and pregnancies were the aggravating factors in only few patients.

Finally from this report it can be said that certain observations are suggestive of the outcome of vitiligo in a patient. Koebner's phenomenon, a family history of vitiligo, presence of autoimmune disorders and mucous membrane involvement showed more progression of vitiligo. Therefore, the ultimate evaluation objective is to be able to choose the appropriate treatment modality and to identify avoidable triggers; such as chemicals, cosmetics, plastics/rubber and subtle trauma on trauma prone sites which may be avoided by wearing adequate clothes and appropriate wears.) In addition from the treatment modalities offered, for the generalized form of the disease in our patients, it can be concluded that all the systemic modalities, oral steroids, PUVASOL and PUVA, are equally efficacious over a period of one year.

In conclusion, the pattern of vitiligo observed in our environment is similar to that reported elsewhere. Clinical characteristics such as family history, clinical type, duration of disease, Koebner's phenomenon, and mucous membrane involvement, were relevant in predicting the progression/ prognosis of vitiligo in South Eastern Nigeria; however further studies still need to be carried out in this area for the region.

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