ORIGINAL ARTICLE (A)

Modification in the frequency of HbS and Hb C in Burkina Faso: an influence of migratory fluxes and improvement of patient health care.

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Abstract

The incidence of hemoglobinopathies (Hb C and Hb S) is relatively high in West Africa. In order to calculate the gene frequency of these hemoglobinopathies, 6619 students of 23 local schools in Ouagadougou (Burkina Faso) and 2582 individuals living in five villages near Ouagadougou, all situated in Savanna, were studied. As expected, the gene frequency in the city schools was 0.111 for β C gene and 0.051 for β S gene, and was 0.122 for β C gene and 0.047 for β S gene in the five villages. This data is somewhat different from that published in a previous study by Labie et al (1984) in the humid Savanna region which showed a higher prevalence of β C (0.14) on β S (0.03), and is in contrast to datat from the arid Sahel region which shows a higher prevalence of β S (0.1) compared to β C (0.05). The higher rate of β S and the lower rate of β C in students in Ouagadougou and in individuals living in the 5 villages near Ouagadougou suggest the possible influence of migratory fluxes of β S from the country region of Sahel. The dramatic increase in the prevalence of HbSS patients, not reported in the study of Labie et al (1984) may be the results of reduced mortality due to environmental change. In addition the improved health conditions of Hb SC and the increased life expectancy of Hb SS may also have facilitated the increase of β S gene and the focus on secondary prevention for the control of correlated disease.

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INTRODUCTION

Burkina Faso is a country situated in West Africa, surrounded by the River Niger, with a population of 12 million, living in an area of 274,200 square kilometres (1). It is an area known for a high rate of two important haemoglobinopathies (Hb C and Hb S). Indeed, it is considered the centre of β C diffusion, and β S is also widely spread; consequently, the frequency of Hb SC compound heterozygotes is quite high. The epidemiology of both hemoglobinopathies has been characterized since 1984 by Labie et al (2), who found in the southern Savanna region (a humid area with 900 mm of rain per year), including the city of Ouagadougou, inhabited specifically by the Mossi, a higher gene frequency of β C (0.14) on β S (0.03). On the other hand, in the northern arid region of Sahel, with rainfall a less than 500 mm a year, and inhabited by several ethnic groups (Songhraïs, Mellebe**,** Peuhl and Touaregs), the gene frequency of β C and β S was inverted (β S 0.1 and β C 0,05 (2). In the above survey the homozygotes for Hb S were not noticed, probably because they died at an early age. Subsequently, Devoucoux et al (3) 1991 who localized the peak of β C gene frequency in the central region of Burkina Faso (Mossi plateau), observed a possible negative correlation between the gene frequencies of β S and β C, which could be due to ethnic migrations or to improved health conditions. From the data collected by Livingston in 1991 (4), it seems evident that, in the last thirty years, a change in the health status and prevalence of the different genotypes has taken place, resulting in a lower frequency of β C and a higher frequency of β S. A careful evaluation of life expectancy of these hemoglobinopathies and of the gene frequencies of β C and β S could provide useful information about the recent changes in social and health conditions of Burkina Faso.

MATERIAL AND METHODS

Samples

The study includes two populations: 1) 6619 selected from 23 local schools in Burkina Faso (age ranging between 10 and 25) were screened for hemoglobinopathies by provision of the Education Minister of Burkina Faso and with the financial support of Conferenza Episcopale Italiana (CEI). 2) 2582 individuals (age ranging between 10 and 45), living in five villages bordering Ouagadougou, were recruited randomly for a screening for hemoglobinopathies with the financial support of CEI.

Methods

All subjects underwent Hb electrophoresis using cellulose acetate plates (Helena) with pH 8.6 buffer. When abnormal hemoglobins were detected, citrate agar electrophoresis at pH 6,4 and a solubility test (to confirm the presence of Hb S and Hb C) were also performed. The percentage of abnormal Hb was measured by gel densitometry with the use of a ADEL 16 (Minivolt) analyser.

RESULTS

Of the 9201 subjects studied, 2770 (30.1 %) showed a β -chain mutation (C or S or both): 141 were heterozygotes for both β C and β S, 94 homozygotes for β C and 12 homozygotes for β S, the remaining were heterozygote for β C (1775) and β S (748). No statistically significant difference in the gene frequencies was found between the Ouagadougou schools (β C 0.111 and β S 0.051) and the villages (β C 0.122 and β S 0.047) (P = 0.225) (see **Table I**). The Hardy-Weinberg statistical values were found to be different between Hb CC, Hb SC and HbSS (see **Table II**). In the schools, the observed frequency of Hb SS and Hb CC was lower than expected (P = 0.004), while in the villages the observed frequency of Hb CC and Hb SC was found higher than expected (P = 0.075).

The median age and range of Hb SS, Hb CC and Hb SC, as an indirect approximate indication of life expectancy for patients with different genotypes, is reported in **Figure 1.** The median age of Hb SS was 9 years and the oldest patients observed were 22 years old. The other genotypes had a median age of 11 and the oldest of them was 42 years old.

DISCUSSION

Of 9201 subjects studied in Ouagadougou schools and in the 5 villages bordering Ouagadougou, 2523 (27.4 %) were heterozygous carriers of haemoglobin mutation (HbS or Hb C), and 247 (2.7 %) were both homozygotes or compound heterozygotes. This study found a slightly increased β S and a decreased β C gene frequency (0.0051 and 0.111 in schools, 0.047 and 0.122 in villages respectively) in the savanna region compared to previously published data (β S 0.03 and β C 0.14) by Labie et al (2). These results were in contrast to those published for the Sahel region (β S 0.105 and β C 0.05) (see **Figure 2**) Two hypothesis could explain the higher percentage of β S, found in schools and villages near Ouagadougou: 1) a migration flow of β S genes following the urbanization process from the Sahel region to the city; 2) an improved life expectancy

of Hb SS and SC, which increase the frequency of Hb S allele. Recently, Segbena et al, 1998 (5), found Hb structural abnormalities in 37% of the 171 newborn Togolese children with a gene frequency of 0.105 for β S and 0.091 for β C, which confirms a good and stable fitness of β S especially in this restricted area of Sahel (South Sahara), which is similar to that of Labie et al in 1984. The inverted correlation between the two gene frequencies of β S and β C found in Sahel and Savanna since 1984 and the intermediate values observed in our study cannot be attributed to the different morbidity of these two hemoglobinopathies in the heterozygote state, but more probably seems to be a consequence of the migration flow (after independence was achived in 1960), from the poorer region of Sahel to the richer Savanna region where Ouagadougou is situated.

In addition the high number of homozygotes for β S, found in both Ouagadougou schools and the villages (12/9201 individuals corresponding to the 0.13 % of all subjects studied) compared with their absence in 1984 data of Labie et al (2), could suggest that the survival of Hb SS patients is improved as a consequence of changes in social and health conditions, such as through the use of antibiotic prophylaxis which has played an important role in establishing a more balanced polymorphism with the Hb S–malaria relationship. The sanitary structure of Burkina Faso has been improved over the past years: CSPS (Healthy Center) have been built in the bigger villages (1972-1976), as have CM (Medical Center, 1979) and CMC (Medical Center with surgery facilities) in all provincies and regions. Moreover the so called Bamako project (1987) which distributes essential drugs at cost price, in particular to women and children has commenced. All these realization have changed the social and sanitary situation of Burkina Faso. The life expectance has increased from 32 years to 52 years, general mortality has decreased from 32 to 16 per 1000 and the infant mortality decreased from 300 to 185 per 1000. The population of Burkina Faso has increased from 10.000.000 to 12.000.000 largerly due to migration from Sahel. The population of Ouagadougou which was 100% Mossi at the time of Independence declaration (1960) became a multiethnic reality, where the marriages are between Mossi and Peulh and Dagari. Alouch, 1997 (6), underlined that the balance between Hb S and malaria is maintained by a higher mortality rate in Hb AAs due to malaria and the high mortality rate of Hb SSs and Hb SCs subjects caused by complications of the disease. However these two hemoglobinopathies may be controlled through earlier detection of patients, who benefit from improved medical assistance

The higher proportion of β S alleles found in schools of Ouagadougou in comparison with villages (0.051 vs 0.047) could also be explained, according to Luzzatto 1979 (7), by the fact that the advantage of Hb S carriers in a malarial region is largely expressed in the early years of life, before immunological defences are built. In fact Chippaux et al (8), in a 1992 study in Benin, found that the prevalence of malaria was not significantly different between AA and AS. However the means of *P. falciparum* parasitaemia were significantly lower in Hb AS children than in Hb AA children (9), suggesting that the

sickle cell trait does not prevent malaria infection, but it is effective in protecting from severe and often fatal attacks of *P. falciparum* cerebral or hepatic malaria, which are frequent during infancy (10).

Another point of consideration is the rather high incidence of β C in Burkina Faso (0.111 in Ouagadougou schools and 0.122 in the villages near Ouagadougou), which could also be explained by an advantage of Hb C heterozygotes over the malaria parasite. However, on this point the results are not always in agreement. In some West African regions with high rate of malaria, children who present Hb AA and Hb AC profiles do not seem to show any evidence of protection by heterozygous state (11). But recently, a case-control study in Dogons of Bandiagara, Mali, has demonstrated that Hb C can protect against severe malaria, but not against infection or uncomplicated malaria (12). The results of that survey suggest not only that a protective effect is associated with Hb C, but that it is greater than Hb S in that part of Africa. Recently Modiano et al. (13), 2001 have demonstrated that Hb C provides protection against clinical *Plasmodium Falciparum* malaria in both the heterozygote (29%) and homozygote state (93%) and it represents the most important factor which maintains the β C gene frequency in Burkina Faso. If we consider that life conditions of homozygous Hb CC are absolutely compatible with normal functions (14), including the reproductive capacity, the vantage of β C on β S may be further improved by the absence of associated pathologies. On the contrary the relatively lower genotypic incidence of Hb SS in Ouagadougou school-children could be a consequence of the higher morbidity of this genotype in the early years of age (15). The difference in the observed versus expected frequency of Hb SS in schools may be due to reduced attendance at school, while the higher observed frequency seen in the villages may be due to recall from the screening campaign. Moreover, it has been suggested that Hb SC individuals have contributed to the persistence and expansion of the β S gene in all countries of the Benin Gulf since their life expectancy is higher than that of SS, and possibly through some resistance to malaria.

If the survival is improved, the clinical status of patients affected by Hb SS remains still precarious in this part of Africa and focus on the priority of secondary prevention of complications associated to this hemoglobinopathy. The development of sickle cell anaemia services, a problem not yet completely solved even in well-faring countries, becomes particularly important now that patients with sickle cell anaemia have a longer life expectancy.

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Table I: Results of Hb electrophoresis and frequencies of Hb alleles concerning the two areas under study.

Hb genotype	Schools* (n. 6619)	Villages** (n.2582)	Total (9201)
AA	4622 (69,83%)	1809 (70.06%)	6431 (69.89%)
AC	1280 (19,34%)	495 (19.17%)	1775 (19.29%)
AS	570 (8,61%)	178 (6.89%)	749 (8.13%)
SC	90 (1,36%)	51 (1.98%)	141 (1.53%)
CC	51 (0,77%)	43 (1,67%)	93 (101%)
SS	6 (0,09%)	6 (0.23%)	12 (0.13%)
Hb alleles	Schools#	Villages##	Total
p β A	0,838	0.831	0.836
q β S	0,051	0.047	0.0496
r β C	0,111	0.122	0.1142
β S + C	0,162	0.169	0.1638

X^2 * →** P= 0.001; X^2 # →## P= 0.255

Table II: Genotypic incidence of β chain mutation according to the places of investigation

	Schools		Villages		Total	
Hb genotype	Ex°	Ob°°	Ex°°°	Ob°°°°	Ex°°°°°	Ob°°°°°°
q2 SS	0,002 (17)	0.0009 (6)	0,002 (6)	0.002 (6)	0.0024 (23)	0.0013 (12)
r2 CC	0,012 (82)	0.008 (51)	0,015 (39)	0.017 (43)	0.0130 (121)	0.0102 (94)
2qr SC	0,011 (75)	0.014 (90)	0,011 (29)	0.020 (51)	0.0113 (104)	0.0153 (141)
2pq AS	0.079 (563)	0.086 (570)	0.078 (200)	0,078 (201)	0.0829 (763)	0.0812 (748)
2pq AC	0.186 (1231)	0.193 (1280)	0.203 (523)	0,192 (495)	0.191 (1756)	0.193 (1775)

X2 °→°° P = 0.004; X2 °°° →°°°° P = 0.075 X2 °°°°° →°°°°°°° P = 0.075??

Ob= Observed frequencies Ex = Expected frequencies

Figure 1: Median ages and relative ranges in different genotypes

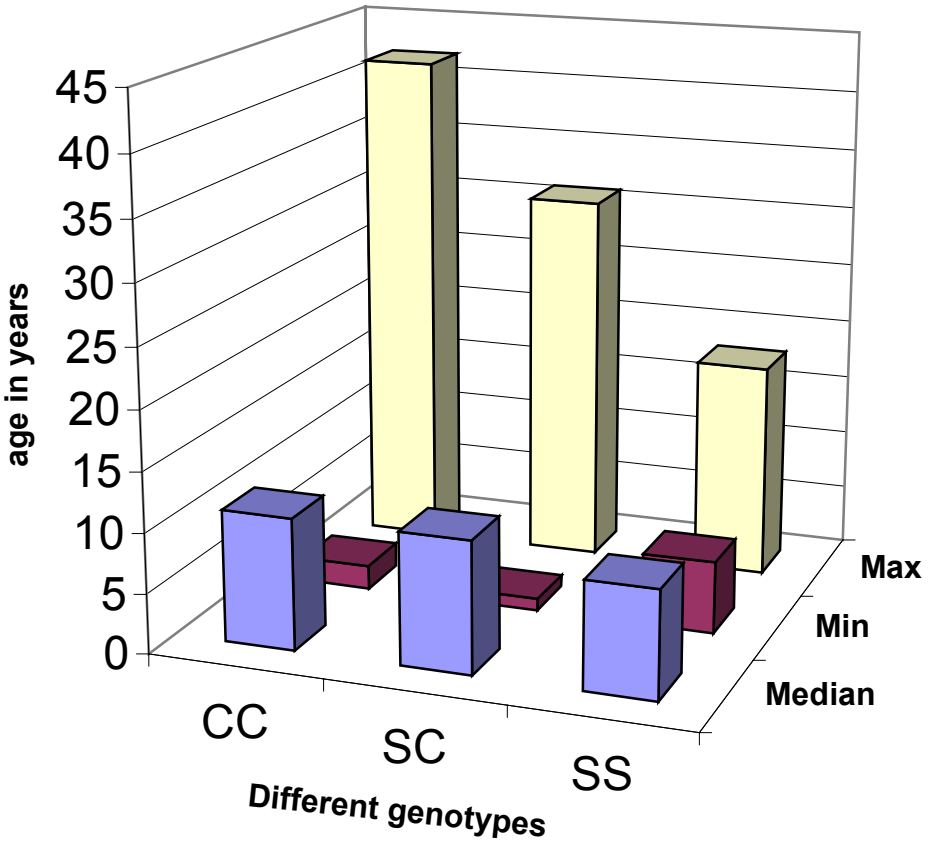

Figure 2: Values of gene frequencies in the schools and villages (2000) in comparison with the values found in the Sahel and Savanna (1984)