Screening for the Sickle Cell Trait in Schools is more Efficient than during the Pre-Nuptial Period for the Prevention of Sickle Cell Anemia in a Sub-Saharan Africa Country. [Sickle Cell Trait Screening and Sickle Cell Anemia Prevention in Sub-Saharan Africa]

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Abstact: Sickle cell disease is a hereditary disease of hemoglobin which has been declared a public health priority by international health decision-making institutions. Among strategies to combat this disease, WHO recommends a reduction of births with sickle cell anemia through awareness and screening for the sickle cell gene in countries where the sickle cell gene is prevalent. Approaches to make this strategy efficient in Sub-Saharan Africa have not been studied. This study aim was to evaluate the efficacy of screening for the sickle cell gene for the primary prevention of sickle cell anemia among two target populations in a country of Sub-Saharan Africa.

This was a prospective study comprising a free and voluntary screening for the sickle cell gene at various intervals, then to evaluate the impact of the screening on engagement or marriage decision-making on two target populations following raising awareness of sickle cell disease. Data was collected through a questionnaire administered at the headquarters of the NGO SS Assistance in Lubumbashi or by phone. 136 pupils with SCT and 111 married couples despite being screened for SCT during engagement were the subject of the study.

In the target group of 136 SCT carriers (AS) in schools, 49 (48%) were married with an AA partner, 53 were engaged among whom 42 with an AA partner, 3 with an AS partner and 8 with a partner with an undetermined hemoglobin phenotype, 34 did not have any commitment. 91 (67%) pupils with SCT avoided a risk for SCA birth. Among the 111 couples married despite their screening as SCT carriers during pre-marital tests, 7 (6, 3%) have not registered SCA birth but 104 (93.7%) had 141 SCA births (extremes: 1 and 3 per couple).

Sickle cell gene screening in a population without engagement or marriage plans is more productive than that conducted in the prenuptial period. However, results highlight the need to conduct more studies on sickle cell gene screening in Sub-Saharan Africa with the best strategies to reduce the psychological, social and economic burden of such studies especially when adults are targeted.

Keywords: Sickle cell trait, Screening, School, Prenuptial, Sickle cell anemia births, Sub-Saharan Africa.

INTRODUCTION

Sub-Saharan Africa and India are regions of the world where the prevalence rates of the sickle cell gene are among the highest in the world [1-3]. The emergence of referral centres for sickle cell disease predicts a future improvement in the medical management of affected individuals with a positive impact on morbidity as well as life expectancy of patients in these two continents. This approach must be reinforced by promoting sensitizing, prevention and early screening of the disease [4-6]. To effectively ensure control of sickle disease, it is imperative that the number of births with sickle cell anemia (SCA) be reduced as a result of screening programmes to detect sickle cell gene carriers and undertake a genetic counseling.

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In order to make these screening programmes more efficient, there is need to clearly define the populations to be screened. To our knowledge, no study has been conducted in Sub-Saharan Africa to address this issue. In theory, two population sub-groups need to be screened: adolescents and prenuptial adults. The aim of the study was to evaluate the effectiveness of screening for sickle cell gene carriers for the primary prevention of sickle cell anemia among school going children and individuals already engaged to be married in a Sub-Saharan African country.

MATERIALS & METHODS

In 2007, awareness-raising meetings followed by prenuptial voluntary sickle cell gene screening were undertaken among 396 engaged couples in the town of Lubumbashi, in the Southern region of the Democratic Republic of Congo. These meetings were followed by a programme to raise awareness of sickle cell disease in 13 schools involving 5829 pupils between September 2008 and April 2009. Of these school children, 1190 pupils aged between 13 and 22 years underwent free and voluntary screening after obtaining parental consent.

In 2013, we measured the level of acquired knowledge on sickle cell disease among pupils who have been sensitized to the sickle cell disease between 2008 and 2009, and we evaluated the attitude of sickle cell trait (SCT) carrier engaged couples who were sensitized in 2007. This activity was conducted using a questionnaire derived from the tool designed by Guedehoussa *et al.* [7] administered in the participants homes, at the NGO (Non-Governmental Organism) SS Assistance offices or by telephone, by a nurse and a final year medical student of the University of Lubumbashi.

Between August 2017 and February 2018, we studied the attitudes of the pupils regarding couple engagement or marriage. Ethical clearance was sought and obtained from the Provincial Health Inspection of Katanga (No 900/1211/BUR.MDC/KAT/2007).

Collected data was entered in Excel 10.0 and analysed using Stata 15.

RESULTS

Results of the Awareness-Raising Programmes and Screening in Schools and Among Engaged Couples

From a population of 5829 pupils sensitized between 2008 and 2009, 1190 underwent free and voluntary screening. 1126 questionnaires were correctly filled in. Among these pupils, 237 (21%) were found to be sickle cell trait (SCT) or heterozygous AS

Table 1: Pupils' Knowledge of Sickle Cell Disease before and after Awareness-raising Programme

Parameters Explored	Before (2008 and 2009) (N=136)	After (2017 and 2018) (N=136)
Cause of sickle cell disease		
Heredity	1 (0.73%)	87 (64.00%)
Parents	8 (5.88%)	49 (36.00%)
Family	0	0
Erroneous response	15 (11.03%)	0
Do not know	112 (82.35%)	0
Biological tool to make diagnosis		
Haemoglobin electrophoresis	2 (1.47%)	136 (100%)
Sicking test	0	0
Blood group determination	88 (64.71%)	0
Do not know	46 (33.82%)	0
Way for primary prevention		
Avoid marriage with haemoglobin defect carrier	3 (2.21%)	136 (100%)
Prenuptial tests (unspecified)	39 (28.68%)	0
Avoid marriage between the same ABO groups	1 (0.73%)	0
Prayer	2 (1.47%)	0
Do not know	91 (66.91%)	0

carriers. 136 of these carriers were investigated further. Out of a population of 396 engaged couples, 138 (34.8%) were diagnosed as sickle cell trait carriers and 111 (93.3%) of these individuals were further investigated for the purpose of this study.

Level of Knowledge about Sickle Cell Disease Among the 136 Sickle Cell Trait Carrier Pupils before and after Awareness-Raising Programme

Table **1** shows that the pupils level of knowledge which was quite poor before the awareness-raising programme improved significantly and in a long-lasting manner, since 64% (95% CI: 55.298-72.019) of the pupils stated that sickle cell disease was a hereditary condition 8 years after awareness compared to 0.73% before awareness. In the same table, it is also clear that 100% of the pupils sensitized to sickle cell disease knew that haemoglobin electrophoresis was the diagnostic test for the disease compared to 1.47% before awareness to the disease. Finally, the results show that all the pupils (100%) felt that haemoglobin electrophoresis was essential in order to avoid marriages between carriers of an abnormal haemoglobin gene.

Attitude of 136 Pupils with Regard to Engagement or Marital Union

During the study period 2017-2018, 34 pupils (25%) among the 136 screened pupils identified as sickle cell trait carriers did not envisage to get engaged or to marry (Figure **1**). Among the remaining 102 pupils, 49 had married a partner with a normal haemoglobin (AA), 53 got engaged (42 with a partner with an AA haemoglobin profile, 3 with an AS partner and 8 with a partner whose haemoglobin profile was undetermined).

Outcome of married couples being screened carrying the sickle cell trait after experiencing sickle cell anemia birth

Figure **2** shows the outcome of the 111 married couples who were screened carrying the sickle cell trait during their engagement after the occurrence of sickle cell births. It is found that 104 (93.7%) have had sickle cell births and 7 (6.3%) have had no children with sickle cell anemia. 13 (12.5%) (95% CI: [6.39 - 19.19]) of the 104 couples who registered births with sickle cell anemia had divorced while 91 (87.5%) had committed to continue their union including 72 couples who have

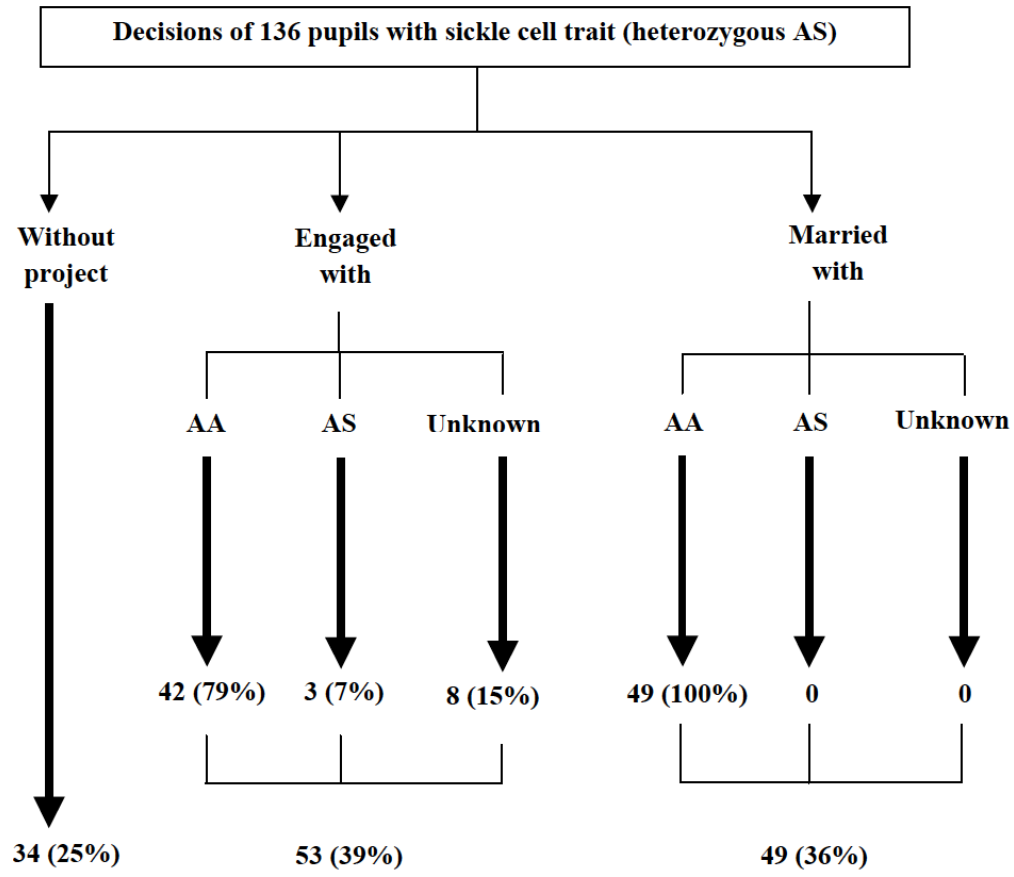

Figure 1: decisions of 136 pupils with sickle cell trait (heterozygous AS).

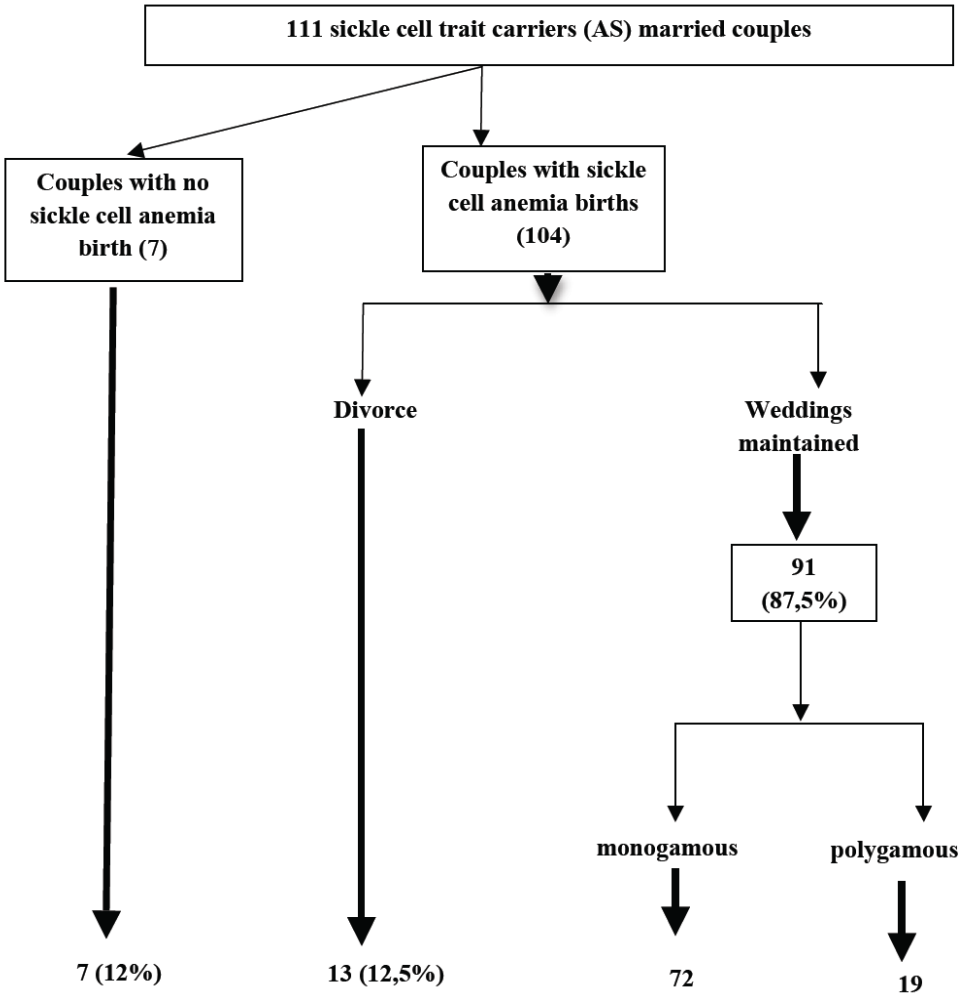

Figure 2: Outcome of the married couples carrying the sickle cell trait (AS) after experiencing a sickle cell anemia births.

preserved its monogamous character but with 19 couples who have become polygamous. Among the men who became polygamous, 18 had married a second wife with normal haemoglobin electrophoresis (AA) and one had married a second wife with sickle cell trait (AS) who had given birth to two children with sickle cell anemia.

Sickle Cell Anemia Prevalence Rate Among the 111 High-Risk Couples who did not Separate after Prenuptial Screening

As shown in Figure **3**, among the 111 couples at risk of having an offspring with sickle cell anemia screened before marriage, only 7 did not have children affected by the disease. From the other 104 couples with sickle cell trait, 141 children were born with sickle cell anemia that is 1 child with sickle cell anemia per couple on average (with up to 3 affected children in extreme cases).

DISCUSSION

To be effective, the fight against sickle cell disease in Sub-Saharan Africa must include two strategies, namely the early screening for sickle cell anemia and the reduction of marriages between sickle cell gene carriers [8, 9]. The efficacy of the second strategy depends on the populations targeted for screening and knowledge acquisition about the sickle cell disease by those screened. After a first study involving 111 couples of engaged adults in 2007 [10], we subsequently focused our attention on school-going children sickle cell trait carriers and without marital intentions, to study the level of knowledge acquired after programmes to arise awareness of sickle cell disease between 2008 and 2009. Results obtained from this population of school children show a good understanding of messages received during the awareness-raising programmes of sickle cell disease since 64% of the participants had permanently acquired an appreciable knowledge about the disease

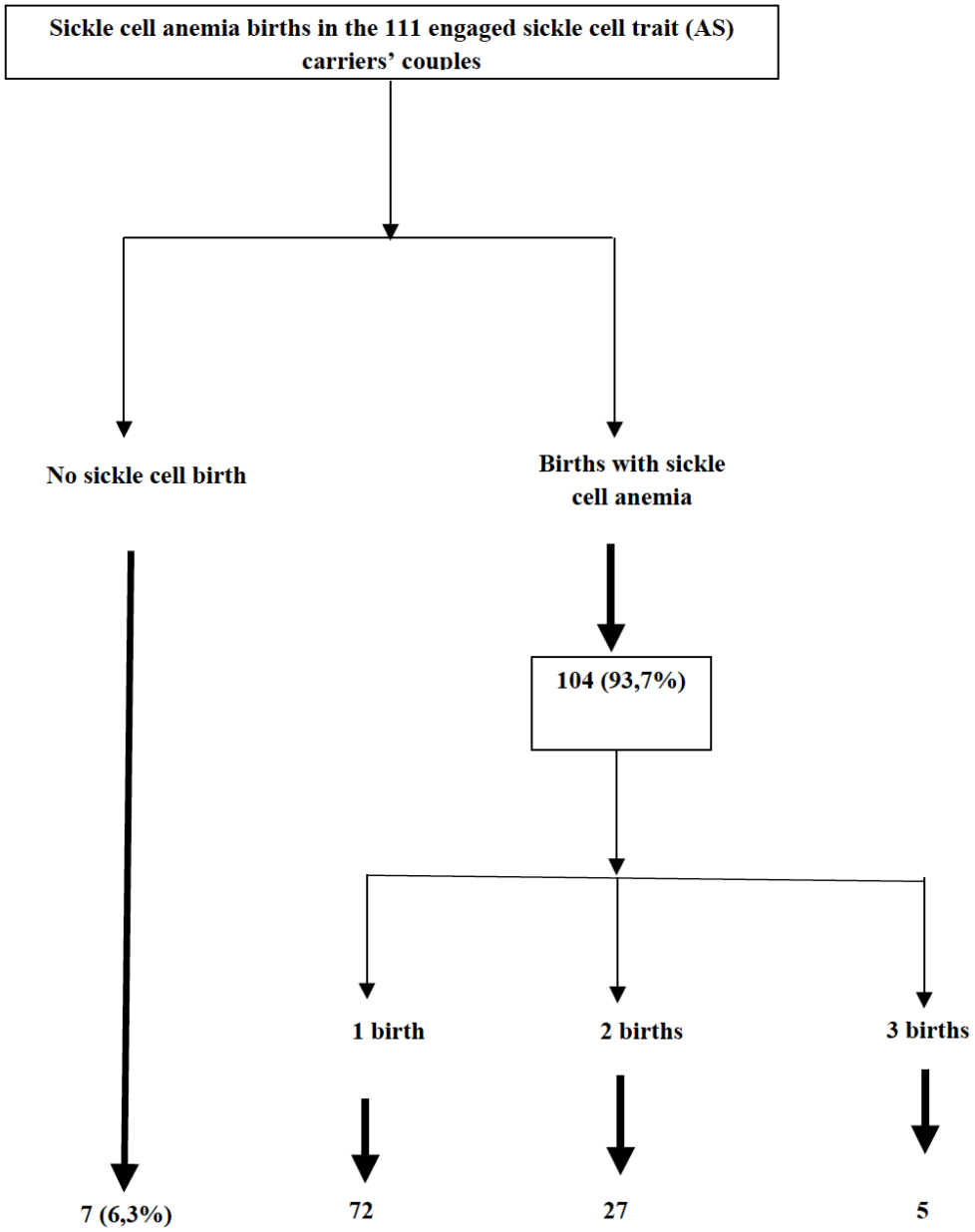

Figure 3: Sickle cell anemia births in the 111 engaged sickle cell trait (AS) carriers' couples ia birth.

transmission and 100% knew how the diagnosis is made. At first glance, there was no indication that the information received by the pupils who were sensitized and screened would in any way truly have an impact on the choice of their future spouse to the point of this having an effect on the status of their offspring. For this reason we conducted a second study 8 years later (2017-2018) to assess the true impact of the awareness-raising programmes and screening approach on the risk of sickle cell anemia births. In the latter study, we found that 36% (42/136) of marriages and 31% (42/136) of engagements involved partners with a hemoglobin AA profile. In the same vein, we evaluated the amplitude of sickle cell anemia among the offspring of the 111 sensitized prenuptial couples at risk of producing sickle cell births. Results obtained from these couples clearly show there was no significant impact in terms of the number of children births with sickle cell anemia.

Indeed, we did observe 84% of marriages among these couples and 141 newborn with sickle cell anemia in these families. We can then conclude that screening of couples at risk before marriage is neither in the short term an efficient preventative approach nor efficacious in this context for the reduction of the incidence of sickle cell anemia. On the other hand, screening for the sickle cell gene among adolescents without marital

intentions is a more efficient preventative strategy. These results however bring up ethical challenges to be address since this is a genetic disease. Indeed, the two approaches explored within the context of this study do not take into account the absence of individual benefit from the screening since the aim is to prevent a disease which does not directly affect the individual concerned even if the birth of a child with sickle cell anemia does affect its parents in many ways, notably psychologically, materially, financially and socially. In this regard, data relative to our 111 at risk engaged couples is revealing in the sense that it shows that 13 (12%) separations led 13 women to become single parent taking care of sick children and 19 polygamous marriages as a result of children being born with sickle cell anemia among the couples. It is then important to give a nuance to the principle of autonomy when it comes to the choice to be made considering long term consequences of decisions that may affect the harmony and the peace of an entire community. Thus, regarding sickle cell carrier individuals already contemplating marriage, it is important to generate ideas on the most efficient means to manage the consequences of the screening results at the social, emotional and economic levels. If currently, this question does not seem to be of utmost importance in developed countries due to good health care systems which have drastically reduced mortality due to sickle cell anemia and significantly improved the life expectancy of sickle cell anemia patients [11-15], the disease is still associated with high levels of morbidity and mortality especially during infancy in resource-poor countries [16, 17]. It is pertinent therefore that programmes be conducted simultaneously on sickle cell gene screening aiming a reduction of the number of births with sickle cell anemia in Sub-Saharan Africa, and studies evaluating the best ways to reduce the psychological, social and economic burden of such screening programmes.

CONCLUSION

The present study explores the question of the best target population to screen in order to reduce marriages at risk of producing an offspring with sickle cell anemia in a Sub-Saharan country. It demonstrates that screening in a school environment in a population without engagement or marriage plans is more productive than that conducted in the prenuptial period. However, the overall results of this study call for the need to conduct more studies simultaneously on the sickle cell trait screening in Sub-Saharan Africa, and the identification of more robust ways to reduce the psychological, social and economic burden of such programmes especially when adults are targeted.

CONFLICT OF INTEREST

Authors declare no conflict of interest.

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