

Estimated Incidence of Sickle-Cell Disease in Aruba and St Maarten suggests Cost-effectiveness of a Universal Screening Programme for St Maarten

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ABSTRACT

Objective: To estimate the incidence of Sickle-Cell Disease (SCD) in Aruba and St Maarten and to determine whether universal screening would be cost-effective according to United Kingdom criteria.

Methods: Consecutive cord blood samples were collected in Aruba and the Dutch part of St Maarten during 3 and 4 months, respectively. Samples were subjected to High Performance Liquid Chromatography (HPLC) screening of haemoglobin variants.

Results: Of the 368 samples (87.6% of all registered births) collected in Aruba, 10 (2.72%; CI 1.3, 4.9%) tested heterozygous for the Sickle-cell gene (HbAS) and 7 (1.90%; CI 0.8, 3.9%) for the haemoglobin C gene (HbAC). Of the 193 samples (83.5%) collected in St Maarten, 14 (7.25%; CI 4.0, 11.9%) contained HbAS and 10 (5.18%; CI 2.5, 9.3%) HbAC. Hardy-Weinberg equilibrium predicted an incidence of 2.65% for HbAS and 1.86% for HbAC in Aruba and 6.80% for HbAS and 4.86% for HbAC in St Maarten. These figures imply a newborn rate of about 2 SCD patients per 3 years in Aruba and 2 SCD patients per year in St Maarten.

Conclusions: Universal screening of newborns for SCD seems cost-effective for St Maarten.

Incidencia Estimada de la Enfermedad de Células Falciformes en Aruba y St Marteen Sugiere Costo-efectividad para un Programa de Pesquisaje Universal para St Marteen

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RESUMEN

Objetivo: Estimar la incidencia de la enfermedad de células falciformes (ECF) en Aruba y St Marteen y determinar si una pesquisaje universal sería costo-efectivo de acuerdo con los criterios del Reino Unido.

Métodos: Se recogieron muestras de sangre de cordón umbilical en Aruba y en la parte holandesa de St Maarten durante 3 y 4 meses, respectivamente. Las muestras fueron sometidas a pesquisaje de variantes de hemoglobina mediante cromatografía líquida de alta eficiencia (CLAE).

Resultados: De las 368 muestras (87.6% de todos los nacimientos registrados) recogidas en Aruba, 10 (2.72%; CI 1.3, 4.9%) resultaron heterocigóticas para el gen de la célula falciforme (HbAS) y 7 (1.90%; CI 0.8, 3.9%) para el gen de la hemoglobina C (HbAC). De las 193 muestras (83.5%) recogidas en St Maarten, 14 (7.25%; CI 4.0, 11.9%) contenían HbAS y 10 (5.18%; CI 2.5, 9.3%) HbAC. El equilibrio de Hardy-Weinberg predijo una incidencia de 2.65% para HbAS y 1.86% para HbAC en Aruba y 6.80% para HbAS y 4.86% para HbAC en St Maarten. Estas cifras implican una tasa de recién nacidos de alrededor de 2 pacientes ECF por año en St Maarten.

Conclusiones: El pesquisaje universal para la detección de recién nacidos ECF parecer ser costo-efectivo para St Maarten.

West Indian Med J 2009; 58 (4): 301

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INTRODUCTION

Aruba (12 30 N, 69 58 W) is a Caribbean island close to the coast of Venezuela. It was once part of the Dutch Antilles but is now a self-governing part of the Kingdom of the Netherlands. The island's first inhabitants were the Caquetios Indians from the Arawak tribe. Contrary to most of the other Caribbean islands, Aruba was spared from slave trade, mainly due to the arid nature of the landscape. From the opening of an oil refinery in 1924, Aruba experienced substantial immigration of workers from other Caribbean islands, who were mainly of African descent. The island is now inhabited by a mixed population of Arawak (Amerindian) descendants, Afro-Caribbeans, Europeans and immigrants from the Caribbean region and South America. St Maarten (18 05 N, 63 12 W) is part of the Dutch Antilles, which forms an autonomous part of the Kingdom of the Netherlands. St Maarten was also originally inhabited by the Arawaks but was found to be uninhabited by the time the Dutch settlers arrived in the 17th century. Slaves were transported to the island to work in the sugarcane plantations during the late 1700s. They originated mostly from the African west coast (1). As opposed to Aruba, St Maarten is currently inhabited mostly by people from Afro-Caribbean descent.

Sickle-Cell Disease (SCD) is a collective term for a group of blood disorders in which pathology is attributed to the inheritance of sickle-cell haemoglobin [HbS] (2). The principal genotypes are homozygous sickle-cell anaemia (SS), sickle-cell haemoglobin C disease (SC) and sickle-cell beta-thalassaemia major ($S\beta^0$) or minor ($S\beta^+$). Sickle-Cell Disease is characterized by haemolysis and vaso-occlusive painful crises which may result in multi-organ dysfunction and an increased susceptibility to infections. Dependent on healthcare facilities, the average life expectancy of patients with SCD may be decreased by 25 – 30 years (3).

The sickle-cell gene is found in people from Africa (or African descent), the Mediterranean area (Italy, Greece), Middle East, East India, Caribbean and Central and South America. Studies show that the HbS and HbC alleles are found at highest frequencies in West Africa where they, together with many other genetic variants (4), have been preserved because of their protection against malaria (5). Sickle-Cell Disease is considered a global health problem and studies show that neonatal screening combined with careful follow-up, adequate parental education and penicillin prophylaxis, considerably reduce morbidity and mortality rates in infancy and early childhood (6, 7).

Universal screening for SCD has been implemented in the United Kingdom (UK), the Netherlands and in most of the United States of America [USA] (8 – 10). Various Caribbean islands such as Jamaica and Curaçao have benefited from screening programmes for SCD (11 – 13). Both Aruba and St Maarten experience an increasing number of immigrants from other Caribbean islands, mainly the Dominican Republic, Haiti and Jamaica. The latter island is known for its relatively high SCD prevalence (11). The aim of the

present study was to estimate the incidence and prevalence of SCD in Aruba and St Maarten and to investigate whether universal screening would be cost-effective, here defined as more profitable compared with targeted screening according to UK criteria (14). We also compared the SCD incidence of Aruba and St Maarten with that of Curaçao (13).

METHODS

Daily collection of EDTA-anticoagulated cord blood samples in Aruba took place from the first of September 2006 until the first of December 2006 (3 months). Collection was enabled with the help of midwives and gynaecologists in the Dr Horacio Oduber Hospital and by a local general practitioner in the Medical Centre. Similarly, cord blood samples were also collected in the Dutch part of St Maarten from the 25th of September 2006 until the 24th of January 2007 (4 months) at the St Maarten Medical Centre. Collection was enabled by the cooperation of local midwives and the participating general practitioners. The study protocol was in agreement with local ethical standards and the Helsinki Declaration of 1975, as revised in 1989. Informed written consent was obtained from all mothers.

The cord blood samples from both Aruba and St Maarten were stored at 4°C for transportation to the Aruba Public Health Laboratory and at -20°C for transportation to the Medical Laboratory Services (Curaçao). High Performance Liquid Chromatography screening for haemoglobin variants was performed as previously described (13). The method enables identification of the structural haemoglobin variants HbS and HbC. No attempts were made to identify α - or β -thalassaemia variants.

Estimates of the incidence and prevalence of SCD in both Aruba and St Maarten were based on the assumption of Hardy-Weinberg equilibrium for the HbA, HbS and HbC alleles, using $(p + q + r)^2 = p^2 + q^2 + r^2 + 2pq + 2pr + 2qr$, where p^2 is the predicted frequency of dominant homozygote (HbAA) in a population, q^2 and r^2 the predicted frequencies of the recessive homozygotes (HbSS and HbCC), $2pq$ and $2pr$ the predicted frequencies of the heterozygotes (HbAS and HbAC) and $2qr$ the predicted frequency of the double heterozygote (HbSC). The predicted frequencies were used to estimate the incidence and prevalence of the above-mentioned genotypes in Aruba and St Maarten, using the numbers of live births per year and the number of inhabitants, respectively. The estimated prevalence of SCD in both Aruba and St Maarten was corrected to account for the lower life expectancy of patients with SCD when compared to that of the general population. Life expectancy data for patients with homozygous sickle-cell disease and sickle-cell-haemoglobin C disease were taken from Platt *et al* (3). Life expectancy data for the general population of both Aruba and St Maarten were provided by the Central Bureau of Statistics of these islands. Data from Curaçao were taken from Van der Dijs *et al* (13) and similarly corrected for the lower life expectancy of patients with SCD. All confidence intervals

(95%) were calculated by means of the exact method (Clopper-Pearson), as based on the binominal distribution (15). The Census registries in both Aruba and St Maarten were helpful in supplying the total number of registered live newborns during the screening period and the total number of registered inhabitants in 2006.

RESULTS

The Census registry of Aruba reported 420 live births during the screening programme, while the Dutch part of St Maarten reported 231 live births. During the screening programme 368 (87.6%) blood samples were collected in Aruba and 193 (83.5%) in St Maarten. We consider these samples representative for the two investigated populations, since we could not identify systematic reasons for the 12 – 16% missing samples. Of the 368 samples collected in Aruba, 17 showed an abnormal haemoglobin profile, of which 10 (2.72%; CI 1.3, 4.9%) exhibited HbAS and 7 (1.90%; CI 0.8, 3.9%) HbAC. Twenty-four of the 193 samples from St Maarten displayed an abnormal haemoglobin pattern, of which 14 (7.25%; CI 4.0, 11.9%) were HbAS and 10 (5.18%; CI 2.5, 9.3%) were HbAC. None of the newborn samples from Aruba or St Maarten displayed homozygosity for haemoglobins S or C, or double heterozygosity (HbSC).

The Hardy-Weinberg equilibrium was used to calculate the incidence and prevalence of the various genotypes in Aruba and Dutch St Maarten. The estimated prevalence was subsequently corrected to account for the higher SCD mortality rate. For this, we used mean life expectancies of the general populations in Aruba and St Maarten of 73 and 74

years, respectively, and life expectancies of 45 and 64 years for HbSS and HbSC, respectively, as established for the USA (3). The Table shows the results together with the genotype frequencies as previously established in Curaçao in 1990 (13) and similarly corrected for lower life expectancy. With an annual birth rate of 1 500 babies in Aruba and 550 babies in St Maarten, these estimates imply the birth of about 2 SCD patients per 3 years in Aruba and 2 SCD patients per year in St Maarten. There might be about 36 SCD patients (12 HbSS and 24 HbSC) among the 106 000 inhabitants of Aruba and about 122 SCD patients (40 HbSS and 82 HbSC) among the 50 334 inhabitants of Dutch St Maarten.

DISCUSSION

St Maarten has 2.6 times higher incidence and 3.4 times higher prevalence of SCD than Aruba, which is in accordance with the higher percentage of Afro-Caribbeans in the St Maarten population. The estimated prevalences for both islands take into account the lower life expectancy of SCD patients. Two studies provide life expectancy data for patients with homozygous Sickle-Cell Disease. There were considerable differences in the outcomes. For the USA, Platt *et al* (3) reported 42 and 48 years for men and women with HbSS, respectively, and 60 and 68 years for men and women with HbSC, respectively. For Jamaica, Wierenga *et al* (16) reported 53 years for men and 58.5 years for women with HbSS, respectively. In the light of the low prevalence, however, these reported differences had little effect on the calculated prevalence from our data. We selected life expectancy data from Platt *et al* (3), since these authors provided data for both HbSS and HbSC patients.

Table: Estimated incidence and prevalence of SCD in Aruba, St Maarten and Curaçao

	Aruba (2006)				St Maarten (2006)				Curaçao (1990)			
	Incidence (no/year)	Per cent	Prevalence	Per cent	Incidence (no/year)	Per cent	Prevalence	Per cent	Incidence (no/year)	Per cent	Prevalence	Per cent
Live births	1552	100	–	100	570	100	–	100	3100	100	–	–
Inhabitants	–	–	106000	100	–	–	50334	100	–	–	145000	100
HbAA	1481	95.43	101160	95.43	501	87.89	44269	87.95	2725	87.90	127455	87.90
HbAS	41	2.65	2814	2.65	39	6.84	3424	6.80	156	5.03	7294	5.03
HbAC	29	1.86	1970	1.86	28	4.91	2446	4.86	208	6.71	9715	6.70
HbSS	0.3	0.02	12	0.01	0.7	0.12	40	0.08	2.2	0.07	61	0.04
HbCC	0.1	0.01	10	0.01	0.4	0.07	34	0.07	3.7	0.12	174	0.12
HbSC	0.4	0.03	24	0.02	1.1	0.19	82	0.16	5.6	0.18	222	0.15
HbSS+HbSC	0.7	0.05	36	0.03	1.8	0.31	122	0.24	7.8	0.25	283	0.20
Allele frequency												
HbA (%)			97.7				93.8				93.8	
Allele frequency												
HbS (%)			1.4				3.6				2.6	
Allele frequency												
HbC (%)			1.0				2.6				3.5	
C/S allele frequency ratio			0.7				0.7				1.4	

Allele frequencies are based on the estimated incidence (Hardy-Weinberg equilibrium). Prevalence was corrected for life expectancy.

A previous report from the UK showed that universal screening for SCD is cost-effective with an incidence of 1.6% HbAS and 0.05% SCD (14). The currently estimated HbAS and SCD incidences in Aruba meet UK criteria, indicating that a universal screening programme would be cost-effective. The reliability of this outcome may however be questioned in the light of the 95% confidence interval (1.3, 4.9%). The incidence estimations of HbAS and SCD for St Maarten are on the other hand well above the criteria, suggesting that institution of a universal screening programme is indicated. There might be various confounders that preclude full comparability with the UK criteria, including the absence of a single screening laboratory and differences in public health services. The introduction of a universal screening programme for SCD that is preferably executed in a single laboratory is indicated. The laboratory might be strategically located in the Caribbean area and support the additional screening for many other severe heritable diseases.

The incidence and prevalence of SCD in Curaçao is higher than in Aruba and St Maarten, but the HbS allele frequency is highest in St Maarten. The HbC/HbS ratio and HbC allele frequency was highest in Curaçao, when compared with Aruba and St Maarten. The HbC gene is estimated to be about 1 000 years old (17). It is considered to be a private gene of the Mossi tribe, which lives in North Ghana/South Burkina Faso (17, 18). Consequently, differences in HbC/HbS ratio and HbS allele frequency are likely to point at differences in the origin of the Afro-Caribbeans in these islands, with a relatively larger part of the Curaçao population deriving from the North Ghana/South Burkina Faso area.

CONCLUSIONS

We conclude that implementation of a newborn sickle-cell screening programme might only be cost-effective for St Maarten. The introduction of a universal screening programme for SCD in a single laboratory that is strategically located in the Caribbean area is indicated and enables screening for other severe heritable diseases.

ACKNOWLEDGEMENTS

We thank the directors and Ms G Balochie-Bonofacio of Medical Laboratory Services (Curaçao) for the analysis of the Hb types of St Maarten. We also thank Dr E Boderie, Mr R Pablo, Ms R Blindeling, Mr G Goeloe, the obstetric practices (Croes and Tromp and Duna Lus) and the nurses of the Horacio Oduber Hospital (Aruba) for their valuable time and efforts and the doctors, nurses and all other workers in

the St Maarten Medical Centre for their cooperation. This study would not have been possible without the aid of the very cooperative parents and their newborns.

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