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Rates and risk factors of hypertension in adolescents and adults with sickle cell anaemia in Tanzania: 10 years' experience

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Summary

Data on the magnitude and risk factors for hypertension in sickle cell anaemia (SCA) are limited. A retrospective analysis of individuals with SCA aged 15 years enrolled from 2004–2014 at Muhimbili National Hospital, Tanzania was conducted to determine the prevalence, incidence and risk factors for hypertension. A total of 1013 individuals with SCA were analysed, of whom 571 (56%) were females. The median age [interquartile range] was 17 [15–22] years. Four hundred and forty-one (44%) of the patients had relative hypertension [systolic blood pressure (SBP) 120–139 mmHg or diastolic blood pressure (DBP) 70–89 mmHg], and 79 (8%) had hypertension (SBP 140 mmHg or DBP 90 mmHg). The incidence of hypertension was 64/1000 person years of observation and the 5-year survival rate was 0.71 [95% confidence interval (CI): 0.67–0.75]. In multivariate analysis, age > 18 years, Hazard ratio (HR) 1.50 (95% CI: 1.03–2.18); pulse pressure,

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The study was conducted by Muhimbili University of Health and Allied Sciences, Dar es Salaam, Tanzania at its teaching hospital, the Muhimbili National Hospital (MNH).

Authorship contributions

All authors contributed significantly to the manuscript and meet the criteria for authorship as follows: AM, BPM, EN, CRN, JL, MTG and JM: designed the study. AM, BPM, MG performed the statistical analysis. AM, BPM, EN, JL, DS, HM, KT, NG, CRN, MTG and JM interpreted data and results. AM, BPM, MN, and JM drafted the first manuscript. All authors commented, revised and approved the final manuscript.

Disclosure of conflicts of interest

All authors have no competing interest to declare.

HR 0.64 (95% CI: 0.42 to 0.98); pulse rate, 1.02 (95% CI: 1.01–1.03); body mass index (BMI), HR 1.08 (95% CI: 1.03–1.13); blood transfusion, HR 2.50 (95% CI: 1.01–6.21) and haemoglobin, HR 1.12 (95% CI: 1.05–1.33) were independently associated with hypertension. In conclusion, despite the younger age, hypertension in this population was higher than that reported in others studies. Age, BMI, pulse pressure and haemoglobin were independently associated with hypertension in SCA.

Keywords

prevalence; incidence; hypertension; sickle cell; Tanzania

The burden of sickle cell anaemia (SCA) is highest in Sub-Saharan Africa (SSA) where 80% of the 300 000 global births of affected individuals live (Weatherall, 2010; Modell & Darlison, 2015). Tanzania is one of the countries that are greatly affected by this condition, with 8000 SCA births per year (Makani *et al*, 2011). The introduction of newborn screening programmes and the improved survival in SCA patients (Platt *et al*, 1994; Lee *et al*, 1995; Quinn *et al*, 2010) have led to the discovery of long-term, age-related complications, such as hypertension.

The pathophysiology of SCA partly involves endothelial dysfunction, a nitric-oxide-deficient state and renotubular ischaemia, events that would be expected to have hypertensive effects. In contrast, several studies have documented that SCA is associated with blood pressure (BP) levels lower or comparable to those of control subjects (Johnson, 1981; Pegelow *et al*, 1997; Gordeuk *et al*, 2008; Desai *et al*, 2012). However, even in a range of systolic and diastolic BPs (SBP, DBP) that could be considered relatively near normal for the general population (pre-hypertensive levels), the risk of cerebral vascular accidents is high in SCA. Data on the prevalence of systolic pre-hypertension in adult patients with SCA is limited but the few available studies show it to range from 38% to 44% (Gordeuk *et al*, 2008; Lamarre *et al*, 2013) although very low prevalences have also been reported (e.g., 1%, Johnson, 1981). In the same studies, a cut-off of SBP 140 mmHg or DBP 90 mmHg, identified a hypertension prevalence of 5–10%. As SSA is undergoing an epidemiological transition, the prevalence of hypertension in the general population is increasing, calling for immediate examination of its magnitude, especially in this specialized population at particularly high risk of developing organ dysfunction.

Risk factors for hypertension are not well known in individuals with SCA; the largest cohort to date (Pegelow *et al*, 1997) included 3317 subjects with SCA and noted a correlation between BP and body mass index (BMI), haemoglobin, measures of renal function and age, although the strength of the association varied between age and sex subgroups. Lamarre *et al* (2013) also found that male sex, triglyceride levels, blood viscosity and BMI were independent risks factors for relative hypertension in sickle cell disease. Understanding the risk factors for hypertension in SCA will lead to preventive and therapeutic interventions targeted for this disease.

Given that the majority of patients with SCA are diagnosed during early childhood or in their youth, we postulated that by as early as adolescent age, many will have accumulated a

sufficient number of risk factors described above to raise the odds of them developing hypertension; perhaps even at younger ages than the general population.

Thus, this study aims to determine the prevalence, incidence and risk factors for hypertension in adolescents and adults with SCA in Tanzania.

Methods

Study design and setting

This is a retrospective analysis of individuals with SCA in the Muhimbili Wellcome Program (MWP) at Muhimbili National Hospital (MNH), in Dar es Salaam, Tanzania. The MNH serves as the main referral hospital in Tanzania. It houses the Muhimbili Sick Cell (MSC) clinic that serves, on average, 30–60 patients per week.

Study population

Individuals with SCA [homozygous haemoglobin SS (HbSS)] aged 15 years or older and prospectively enrolled in the Muhimbili Sick Cohort between 2004 and 2014 were included. Individuals with a medical history suggestive of SCA were identified at the paediatric or haematology clinics or during hospitalization and screened for SCA. Those individuals confirmed to have SCA were enrolled into the MSC clinic, where detailed clinical and laboratory information are collected. Follow-up visits are scheduled every 3–9 months. Care and monitoring is provided to individuals with SCA following national and hospital treatment guidelines as follows: Penicillin V is given to all SCA individuals under 5 years of age, and folic acid and deworming is provided to all SCA individuals, irrespective of their age. Patients with a haemoglobin of <50 g/l or acute drop in haemoglobin >20 g/l below steady state or severe anaemia with heart failure receive a top-up blood transfusion at a dose of 10 ml/kg. Patients with fever undergo full blood picture and malaria test, chest-X-ray, urine and blood culture and initially receive broad-spectrum antibiotics while waiting for microbial identification. Individuals with painful crisis receive the following depending on severity of pain: mild pain: paracetamol 15 mg/kg 6-hourly; moderate pain: paracetamol 15 mg/kg 6 hourly and ibuprofen 5 mg/kg 8-hourly or diclofenac 1 mg/kg 8-hourly; severe pain: oral morphine 500 µg/kg 4-hourly.

Clinical data

At baseline, demographic information is provided by individuals with SCA. Clinical data collected include history of sickle cell disease, blood transfusion, anthropometric measurements, oxygen saturation, BP, pallor, jaundice and presence of splenomegaly. Blood pressure readings were obtained by physicians according to a standard protocol recommended by the World Health Organization at study enrolment and at follow-up (WHO, 2015). For each participant, BP was measured in the right arm in a seated position, having rested for at least 5 min, using an OMRON digital automatic BP monitor (OMRON-4, Omron Corporation, Kyoto, Japan) with an appropriate cuff size.

Outcome measures

The primary outcome was baseline hypertension and the second outcome was incident hypertension. Baseline hypertension was defined as SBP \geq 140 mm/Hg or DBP \geq 90 mmHg recorded at enrolment. Incident hypertension was based on having at least one of the following criteria: two readings of SBP \geq 140 mm/Hg or DBP \geq 90 mmHg or one reading of SBP \geq 140 mm/Hg or DBP \geq 90 mmHg plus one reading of SBP 120–139 mmHg or DBP 80–89 mmHg, as measured at two follow-up clinic visits in those who were normotensive at entry into the study.

Laboratory methods

Patients underwent alkaline haemoglobin electrophoresis (Helena, Sunderland, Tyne & Wear, UK) for determination of HbAA, HbAS and HbSS status. Confirmation of sickle phenotype and quantification of HbF was performed by High Performance Liquid Chromatography (HPLC) (Variant Analyser, Bio-Rad, Hercules, CA, USA). All samples were processed in the Central Pathology Laboratory of MNH.

Ethical approval

The study was approved by the ethical committee of the Muhimbili University of Health and Allied Sciences (reference MU/RP/AEC/VOL XI/33). Written informed consent, in the local language (Kiswahili), was obtained from parents or guardians of children and from patients who were \geq 18 years old.

Statistical methods

Information was checked for consistency before double entry into a database written in MySQLv5.0 (Sun Microsystems Inc, Santa Clara, CA, USA). STATA 14 (Stata Corp, College Station, TX, USA) and R3.2.2 (<http://www.R-project.org/>) were used for analysis. The Muhimbili Sickle Cohort is a prospective, longitudinal cohort of individuals with SCA who attend repeated follow-up clinic visits. Continuous variables were presented as median (interquartile range) and categorical variables as percentage. The prevalence of hypertension at baseline was presented as the proportion of patients with SCA based on the BP determined at study entry into the cohort. As per Seventh Report of the Joint National Committee on prevention, evaluation and treatment of high BP guidelines (Bakris *et al.*, 2012), patients were categorized as having normal BP (SBP $<$ 120 mmHg and DBP $<$ 80 mmHg), relative hypertension (SBP 120–139 mmHg or DBP 80–89 mmHg) or hypertension (SBP \geq 140 mmHg or DBP \geq 90 mmHg) based on the baseline values. Based on the European hypertension guideline (Mancia *et al.*, 2007), further BP cut-offs for the analysis included SBP \geq 130 or DBP \geq 85 mmHg, SBP \geq 160 or DBP \geq 100 mmHg and SBP \geq 180 or DBP \geq 110 mmHg. Based on the definition above, the overall incidence of hypertension was determined as number of individuals who experienced events during the defined follow-up period divided by the total time under follow-up. Categorical variables were compared using χ^2 -test or Fisher exact test if the expected count in one of the cells was less than five while continuous variables were compared according to BP category with the Kruskal–Wallis test. The event-free probability from incident hypertension was assessed by Kaplan–Meier plots. Cox regression analyses were used to assess the risks of incident hypertension.

Variables with $P < 0.10$ and, additionally, age and sex were included in the multivariate analysis. A two-sided P value of 0.05 was considered statistically significant.

Results

Baseline characteristics and prevalence of hypertension

Table I shows the socio-demographic, clinical and laboratory characteristics by BP category. A total of 1013 individuals with SCA were available for analysis, of whom 571 (56%) were females. At baseline, the median age [interquartile range] was 17 [15–22] years, ranging from 15 to 59 years. Approximately half of the patients (476 or 48%) were normotensive, 441 (44%) had relative hypertension and 79 (8%) had hypertension. Age was significantly different across BP categories, with age increasing with hypertensive grade ($P < 0.001$), while sex was not ($P = 0.295$). Interestingly, the proportion of patients with oxygen saturation $>95\%$ was increased in the relative hypertension group and further increased in the hypertensive group ($P = 0.020$) as compared to the normotensive group. Pulse rate ($P = 0.020$), BMI ($P = 0.022$), haemoglobin ($P < 0.001$) and lactate dehydrogenase ($P = 0.013$) were also significantly different across the three BP categories.

Using various cut-off values, the prevalence of SBP ≥ 130 or DBP ≥ 85 mmHg was 13% (95% confidence interval [CI]: 11.1–15.3), SBP ≥ 140 mmHg or DBP ≥ 90 mmHg was 8.0% (95% CI: 5.5–10.5), SBP ≥ 160 or DBP ≥ 100 mmHg was 2.0% (95% CI: 1.1–2.8) and SBP ≥ 180 or DBP ≥ 110 mmHg was 1.6% (95% CI: 0.8–2.4), Fig 1. After subgroup analysis in patients' aged ≥ 18 years, the crude prevalence of hypertension (SBP ≥ 140 mmHg or DBP ≥ 90 mmHg) was found to be 5.3%.

Incidence and event free from hypertension

The median duration of follow-up was 8.9 years. A total of 203 events occurred during 3145 person-years of follow-up, giving an overall incidence rate of 64/1000 person years. The 1-year event-free survival from incident hypertension was 0.95 (95% CI: 0.93–0.97) and the 5-year survival was 0.71 (95% CI: 0.67–0.75), Fig 2A. The 1-year survival rates for patients aged ≥ 18 years vs. <18 years were 99% vs. 93% ($P < 0.001$), Fig 2B.

Risk factors for overall incident hypertension

Table II shows the predictors of incident hypertension. As observed in the multivariate analysis, the variables predicting incident hypertension in the univariate analysis remained significant in the overall multivariate analysis: age ≥ 18 years, Hazard ratio 1.75 (95% CI: 1.04–2.92); blood transfusion, 2.88 (95% CI: 1.15–7.20); pulse rate 1.02 (95% CI: 1.01–1.04); pulse pressure 1.03 (95% CI: 1.02–1.05); BMI, 1.08 (95% CI: 1.03–1.14) and haemoglobin, 1.21 (95% CI: 1.07–1.36). Sex, painful crisis, splenomegaly, worsening jaundice and oxygen saturation were not associated with hypertension. In a separate analysis among individuals ≥ 18 vs. <18 years (Table III), radial pulse and pulse rate were the only variables associated with incident hypertension in both groups (both $P < 0.05$). The BMI [1.08 (95% CI: 1.02–1.15)] and haemoglobin [1.18 (95% CI: 1.04–1.35)] were also associated with hypertension in those aged ≥ 18 years but not in those <18 years of age.

Results from Cox regression models showed the linear relationship between age and BMI with hypertension ($P=0.761$ and $P=0.217$, respectively).

Discussion

This study provides clinically important information on the burden of hypertension in a large cohort of adolescent and adults with SCA in a Sub-Saharan country. The incidence of hypertension in SCA patients was found to be 64 per 1000 person years of observation. Advancing age, radial pulse, pulse pressure, increasing BMI and haemoglobin were independent predictors of incident hypertension. Most of these conditions are possible to detect and control in a way that would impact on the incidence of hypertension amongst persons with SCA in Tanzania.

Despite the fact that SCA is invariably accompanied by both structural and functional renal abnormalities in adults, one might expect its magnitude to be higher in these individuals than in the general population, however the current findings confirm the previous reports that the prevalence and incidence of hypertension in individuals with SCA is of low magnitude even in situations where age/sex were comparable (Johnson, 1981; Pegelow *et al*, 1997; Gordeuk *et al*, 2008; Lamarre *et al*, 2013). In this study the prevalence of 5.3% in individuals >18 years was also much lower as compared to 19% (>18 years) in the general Tanzanian population (Hendriks *et al*, 2012). This association between low prevalence of hypertension and SCA may be related to premature deaths in patients with SCA in which early death could remove those individuals whose BP might reach hypertensive levels by middle adulthood (Johnson, 1981). The other explanation is that lower systemic BPs in SCA may be a result of higher urinary sodium loss due to hyposthenuria (Johnson, 1981; Pegelow *et al*, 1997). Despite the younger age (mean 20 years) of individuals in the current study, the overall prevalence of hypertension of 8% was slightly higher than the study conducted by Lamarre *et al* (2013) in which it was 5% in a population of with a mean age of 33 years, and a similar prevalence (10%) in a study conducted by Gordeuk *et al* (2008). Furthermore, the prevalence of pre-hypertension in these studies was similar to the current study. The possible explanation for higher prevalence at a younger age in this study compared to that reported by Lamarre *et al* (2013) might be due to better health services for SCA patients and the general population in the developed world, thus experiencing less the frequency of infections, dehydration and blood volume expansion. The cohorts from developed countries (Pegelow *et al*, 1997; Lamarre *et al*, 2013) showed a clear positive correlation between BMI and BP. In the current cohort, as compared to resource-rich countries, there are might be a survival bias in the SCA patient populations. It is likely that the patients with SCA who survive to adulthood and are included in this study are those that have better nutritional status, higher BMI and, consequently, higher BP. Whether the high rate of painful crises (possibly resulting from frequent infections, dehydration) in the current study [>2 episodes in 35% of those with hypertension vs. any episode in 16% of hypertensive individuals in the study of Lamarre *et al* (2013)] plays a role in this high rate of hypertension, remains largely unknown.

The possible explanation for younger age in Tanzania (one decade less compared to studies in developed countries) is unknown, although it might be a reflection of the general

population, in which hypertension and heart failure affect a younger population, in most SSA countries as compared to developed countries (Tibazarwa *et al*, 2009; Damasceno *et al*, 2012; Ogah & Rayner, 2013; Makubi *et al*, 2014).

Comparisons of incidence rates with those from other contemporary studies in SCA are limited. However, in the general population, the incidence of hypertension is higher in most countries (Kiefe *et al*, 1997; Hajjar *et al*, 2006; Gabriel *et al*, 2014). The underlying mechanisms for low magnitudes of hypertension incidence in SCA might be attributed to salt-losing enteropathy (Pegelow *et al*, 1997; Gordeuk *et al*, 2008) and the role of nitric oxide, as previously reported (Gordeuk *et al*, 2008).

Advancing age is well known to be associated with hypertension in the general population. The current study confirms this finding, even in a SCA cohort, a similar finding reported in developed countries (Pegelow *et al*, 1997; Desai *et al*, 2012) and in Africa (Akingbola *et al*, 2014). With the improved survival of patients with SCA, the incidence of hypertension is expected to rise, thus screening and awareness are required to prevent the expected complications.

The present finding of a significant role of BMI in hypertension in a population with a mainly low BMI has important public health implications. Thus, increased BMI in SCA might also contribute to the modulation of BP (Desai *et al*, 2012). This finding is consistent with other studies in developed countries (Homi, 1993; Pegelow *et al*, 1997; Lamarre *et al*, 2013).

Increasing haemoglobin and blood transfusion were additional independent risk factors for hypertension suggesting a need for more understanding of the pathophysiological factors. The correlation between increasing haemoglobin and hypertension has also been reported by Pegelow *et al* (1997), and is partly due to the increased viscosity resulting from the increased numbers of erythrocytes (Johnson, 2005). Likewise, and consistent to our findings, in Nigeria, Oguanobi *et al* (2010) found an association between hypertension and history of blood transfusion, which may indicate a more severe phenotype. Furthermore, in this cohort where patients depend on top-up blood transfusion instead of exchange transfusion, the chances of both volume expansion and increased haemoglobin levels are high and possibly predispose these patients to hypertension.

Elevated pulse pressure is currently known to be an independent predictor of morbidity and mortality in patients with cardiovascular diseases [reviewed in Dart and Kingwell (2001)] but comparable data in SCA patients is limited. The current study found that elevated pulse pressure was associated with incident hypertension. Patients with SCA tend to have elevated pulse pressure compared to controls (Oguanobi *et al*, 2010) but its association with hypertension has not been well documented, except in the general population, particularly the elderly, whose aortic wall stiffness greatly contributes to the pathogenesis (Nichols *et al*, 1992; O'Rourke & Nichols, 2005). 'In the current young study population, the association between pulse pressure and hypertension might be related to increased stroke volume as a compensatory mechanism, similar to that in patients with chronic haemolytic anaemia (Novelli *et al*, 2014).

The strength of the present study is that it is based on a large and well-characterized homozygous study population in a resource-limited country. This expands the understanding of hypertension in SCA beyond what has been reported from developed countries.

There are limitations to this study, such as being conducted in an urban referral hospital. Thus, the findings may not be representative for hypertension seen in rural SSA. However, the study still provides a comprehensive evaluation of hypertension with key risk factors for intervention in countries with limited resources.

In conclusion, given the young age of the patients in this cohort, the prevalence of hypertension was high compared to other most studies, but with low incidence, which was strongly associated with age, BMI, blood transfusion and haemoglobin level. Hypertension must be seen as a prioritized target for early detection and intervention. Proper monitoring of body weight, blood transfusion and haemoglobin moderation may favourably impact on the incidence of hypertension.

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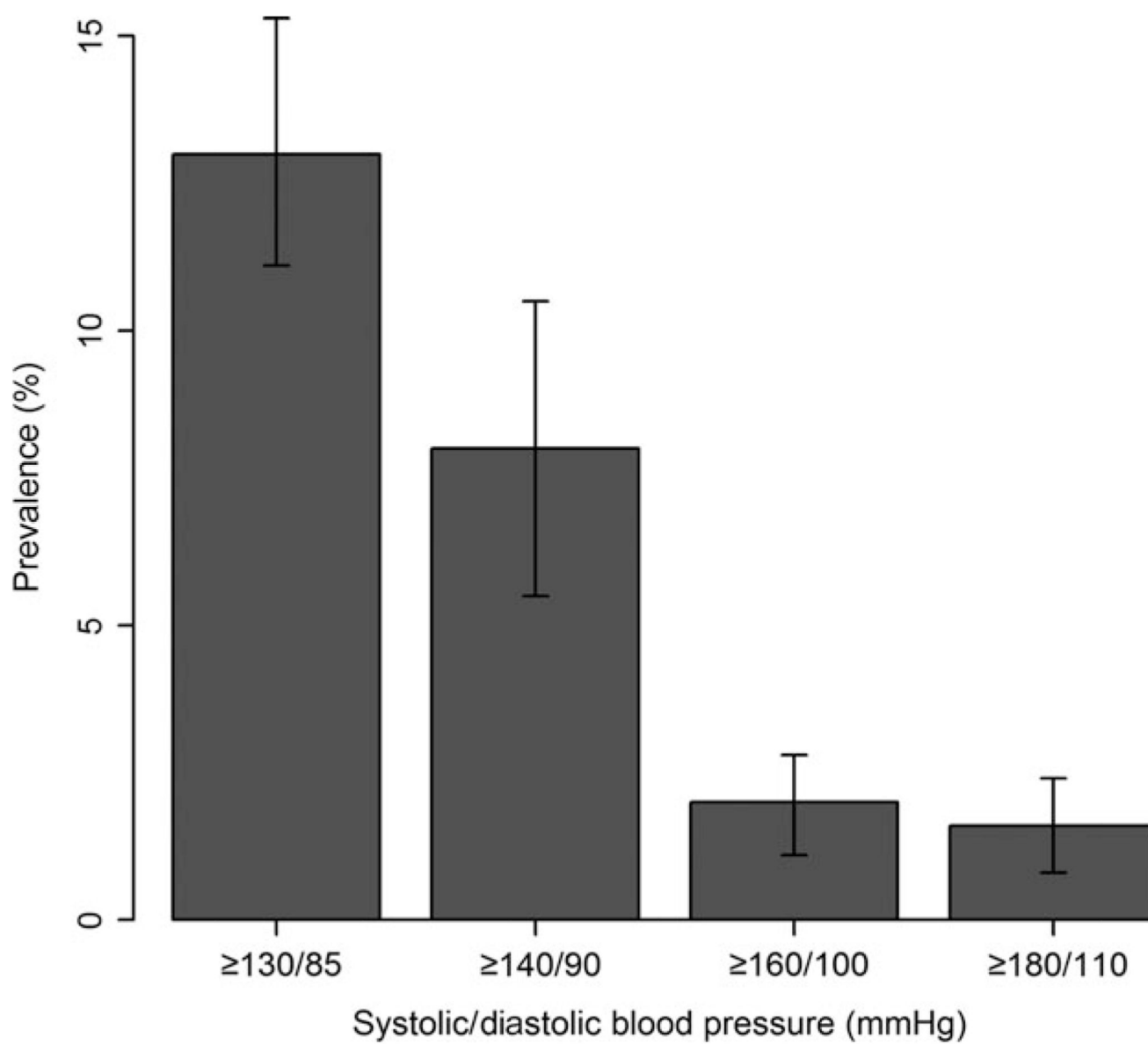
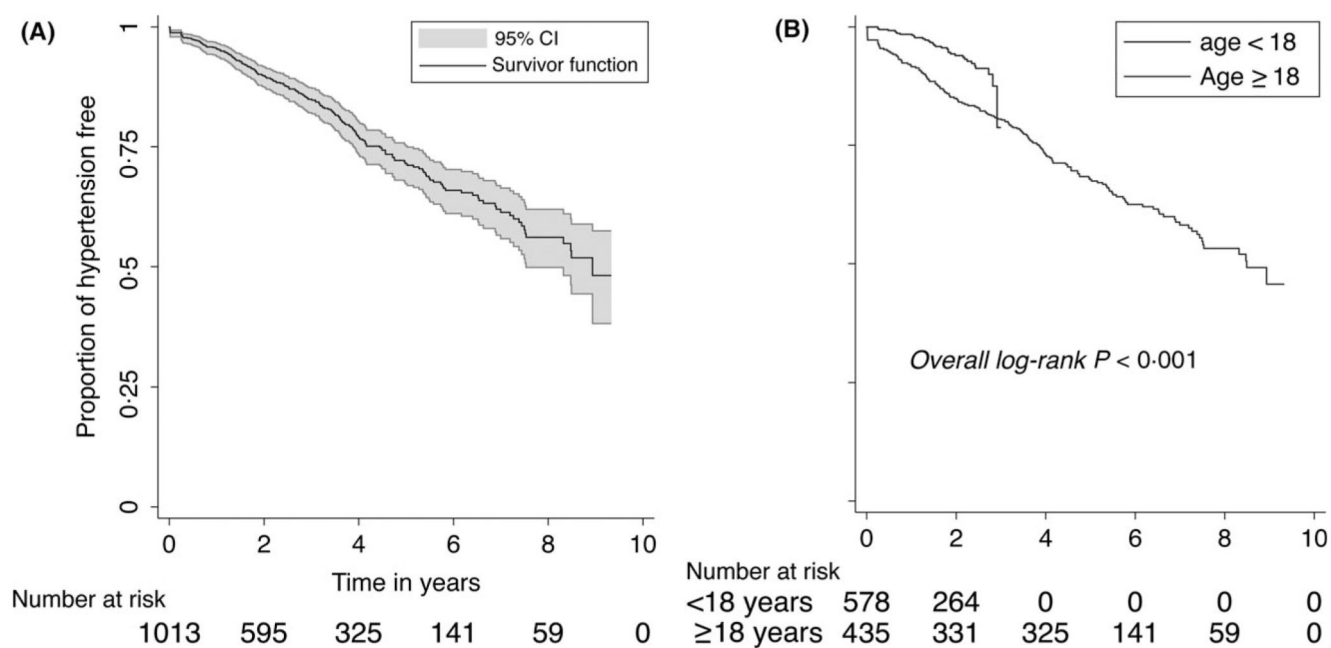


Fig 1.
Baseline prevalence of hypertension (at various systolic/diastolic blood pressure cut-offs).

**Fig 2.**

Kaplan-Meier curve for the incident hypertension (A) overall (B) by age group.

Table I

Baseline demographic, clinical and laboratory characteristics of individuals with SCA aged 15 years by blood pressure levels.

	SBP < 120 and DBP <80 mmHg (n = 476)		SBP 120–139 and/or DBP 80–89 mmHg (n = 441)		SBP 140 and or DBP 90 mmHg (N=79)		
Characteristics	Median/n	IQR/%	Median/n	IQR/%	Median/n	IQR/%	P-value
Demographics							
Female sex	272	56.9	237	53.6	49	62.0	0.295
Age, years	16	15–20	18	15–23	21	17–25	<0.001
<18 years	324	68	240	54	26	33	<0.001
18 years	152	32	201	46	53	67	
Clinical							
Febrile episodes (>2)	207	30	75	27	9	24	0.542
Painful episodes (>2)	126	35	92	33	17	43	0.443
Blood transfusion (any)	44	12	36	23	5	13	0.970
Central nervous event	3	0.8	3	1.1	1	2.5	0.507
Splenomegaly	19	5.8	18	5.9	1	1.6	0.489
Worsening jaundice	18	5	7	2.5	3	7.5	0.104
Leg ulcer	4	1.3	0	0	1	3.5	0.088
Oxygen saturation	98	96–99	98	96–100	99	96–100	0.112
>95%	384	81	381	87	71	90	0.020
95%	92	19	60	13	8	10	
Radial pulse (beats/min)	84	77–92	85	77–96	89	79–98	0.0219
Body mass index (kg/m ²)	17.4	14.6–18.3	19.4	17.2–20.2	19.1	17.0–19.7	<0.001
Laboratory							
White blood cell count (×10 ⁹ /l)	12	10–15	12	9–15	12	10–14	0.557
Haemoglobin (g/l)	73	74–81	83	73–90	82	71–93	<0.001
Haemoglobin F (%)	5	3–8	4	2–8	4	2–6	0.857
Mean corpuscular volume (fl)	82	75–88	83	75–89	85	75–89	0.305
Red cell distribution (%)	21	19–24	21	19–24	20	18–23	0.007
Reticulocyte count (%)	11	7–16	10	7–15	10	7–14	0.694
Aspartate aminotransferase (u/l)	41	24–54	42	30–57	41	28–55	0.482
Bilirubin-total (μmol/l)	60	27–107	61	35–103	62	30–125	0.364
Bilirubin-indirect (μmol/l)	15	8–24	16	10–23	18	10–21	0.483
Lactate dehydrogenase (u/l)	665	365–1087	881	549–1203	668	500–1057	0.013

DBP, diastolic blood pressure; IQR, interquartile range; SBP, systolic blood pressure; SCA, sickle cell anaemia.

Table II

Predictors of incident hypertension in patients with SCA.

Characteristic	Univariate			Multivariate		
	HR	95% CI	P-value	HR	95% CI	P-value
Demographics						
Sex (female)	1.02	0.77–1.34 *	0.906	0.99	(0.67–1.45)	0.980
Age (years)						
<18 years		1				
18 years	2.23	1.48–3.39 *	0.000	1.75	(1.04–2.92)	0.034
Clinical						
Febrile episodes (>2)	0.71	0.49–1.03 *	0.069	0.68	(0.44–1.05)	0.083
Painful episodes (>2)	0.83	0.59–1.16	0.268			
Blood transfusion (any)	2.56	1.44–4.56 *	0.001	2.88	(1.15–7.20)	0.023
Splenomegaly	1.59	0.64–3.94	0.316			
Worsening jaundice	0.82	0.21–3.31	0.781			
Leg ulcer	0.62	0.09–4.44	0.637			
Oxygen saturation						
>95%		1				
95%	0.96	0.65–1.41	0.844			
Radial pulse (beats/min)	1.02	1.01–1.02 *	0.002	1.02	(1.01–1.04)	0.001
Pulse pressure (mmHg)	1.03	1.02–1.05	0.000	1.03	(1.02–1.05)	0.000
Body mass index (kg/m ²)	1.09	1.05–1.13 *	<0.001	1.08	(1.03–1.14)	0.003
Laboratory						
White blood cell count ($\times 10^9/l$)	0.99	0.97–1.02	0.754			
Haemoglobin (g/l)	1.21	1.09–1.34 *	<0.001	1.21	(1.07–1.36)	0.003
Mean corpuscular volume (fl)	1.00	0.99–1.01	0.634			
Red cell distribution (%)	1.00	0.97–1.05	0.616			
Reticulocyte count (%)	1.00	0.98–1.02	0.885			
Aspartate aminotransferase (u/l)	1.00	0.99–1.01	0.681			
Bilirubin-total ($\mu\text{mol/l}$)	1.00	0.99–1.00	0.865			
Bilirubin-indirect ($\mu\text{mol/l}$)	0.99	0.96–1.02	0.541			
Lactate dehydrogenase (u/l)	0.99	0.99–1.00	0.610			

95% CI, 95% confidence interval; HR, hazard ratio; SCA, sickle cell anaemia.

*
Included in the multivariate analysis.

Table III

Predictors of incident hypertension in patients with SCA, by age category.

Characteristics	Multivariate 18 years			Multivariate <18 years		
	HR	95% CI	P-value	HR	95% CI	P-value
Demographics						
Sex (female)	1.14	0.74–1.74	0.554	0.60	0.22–1.58	0.297
Clinical						
Febrile episodes (>2)	0.75	0.48–1.18	0.215	0.41	0.12–1.39	0.151
Radial pulse (beats/min)	1.02	1.00–1.03	0.014	1.05	1.02–1.08	0.003
Pulse pressure (mmHg)	1.02	1.02–1.05	0.000	1.04	1.01–1.07	0.017
Laboratory						
Body mass index (kg/m ²)	1.08	1.02–1.15	0.009	1.10	0.95–1.28	0.186
Haemoglobin (g/l)	1.18	1.04–1.35	0.014	1.12	0.80–1.57	0.491

95% CI, 95% confidence interval; HR, hazard ratio; SCA, sickle cell anaemia.