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Short Communication

Population Screening for Sickle Cell Trait Among Blood Donors in Multiethnic Urban Centers

Bartko M[1*], Krejcirik B[2] and Szabo I[3]

[1]Department of Cellular Therapy and Transplantation, Meuse Center for Transfusion Sciences, Portugal

[2]Department of Laboratory Hematology, Garonne Center for Leukemia and Lymphoma Studies, Ukraine

[3]Department of Laboratory Hematology, Iskar Institute of Clinical Coagulation Medicine, Poland

*Address for Correspondence: Miriam Bartko, Department of Cellular Therapy and Transplantation, Meuse Center for Transfusion Sciences, Portugal; E-mail: miriam.bartko@meuse.edu

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Abstract

Background: Sickle cell trait (HbAS) carrier frequency is highest in donor communities with West African, Afro-Caribbean, South Asian, and Latin American ancestry, populations well represented at multiethnic urban blood centers.

Objective: To synthesize published evidence on sickle cell trait prevalence among blood donors, the methods used to detect it, and the clinical and ethical issues raised once a donor's status is known.

Methods: Narrative synthesis of peer-reviewed prevalence surveys, donor-safety evaluations, and cohort studies of exertional, thrombotic, and renal outcomes associated with sickle cell trait.

Findings: Reported donor prevalence ranges from under 2% to over 11% depending on population, and carriers show modestly elevated risk of exertional rhabdomyolysis, venous thromboembolism, and chronic kidney disease without excess all-cause mortality.

Conclusions: Blood services increasingly surface sickle cell trait as an incidental finding and need a shared standard for counseling and notification that is decoupled from donor eligibility.

Keywords: sickle cell trait; blood donors; hemoglobinopathy screening; transfusion medicine; donor notification

1. Introduction

Sickle cell trait, the heterozygous carriage of one hemoglobin S allele (HbAS), is usually described to patients as a benign carrier state, distinct from sickle cell disease and requiring no treatment. That description is basically correct for day-to-day health, and it stands in contrast to sickle cell disease itself, a severe multisystem disorder of hemoglobin polymerization and vaso-occlusion [1,2], but the trait's status as an entirely benign carrier state has become less secure over the past fifteen years as large cohort studies have attached it to a modest but real excess of venous thromboembolism, chronic kidney disease, and exertion-related complications [3]. Blood collection agencies sit at an unusual intersection of this evidence: they draw from exactly the multiethnic urban populations in which HbAS carrier frequency is highest, they already perform hemoglobinopathy-adjacent testing for other reasons, and a growing number of them now return sickle cell trait results to donors as an incidental finding rather than as a targeted screen. The result is that transfusion services in cities with large West African, Afro-Caribbean, South Asian, Mediterranean, and Latin American donor bases are, in effect, running an opportunistic population-screening program without having necessarily set out to build one.

This short communication draws together what is known about the prevalence of sickle cell trait in donor populations, how blood services have approached detection and reporting, and what the clinical and ethical stakes are once a donor's status becomes known. The aim is not to argue for or against a specific screening policy but to lay out, concisely, the evidence a transfusion medicine program needs before deciding how to handle a result that a growing share of its donors will eventually generate.

2. Prevalence of sickle cell trait across donor populations

The global distribution of HbAS mirrors the historical range of falciparum malaria, with allele frequencies reaching their highest values across a belt running through West and Central Africa and lower peaks around the Mediterranean, the Arabian Peninsula, and parts of the Indian subcontinent [4]. Migration has carried that distribution into cities far from these belts, which is precisely why donor centers in multiethnic urban catchments now see carrier frequencies that would be unremarkable in Lagos or Kinshasa but are notably higher than a national average. A cross-sectional screen of 150 donors at a teaching hospital in Cape Coast, Ghana, found 17 carriers, a prevalence of 11.3% [5], consistent with rates reported across sub-Saharan African donor services generally. At the other end of the range, a Brazilian donor cohort of 7,166 first-time donors screened at a regional hemocenter found sickle cell trait in 127 individuals, or 1.77%, a figure the authors situated within a national range of 0.4-3.42% but well below the 11-13% typical of sub-Saharan African series [6].

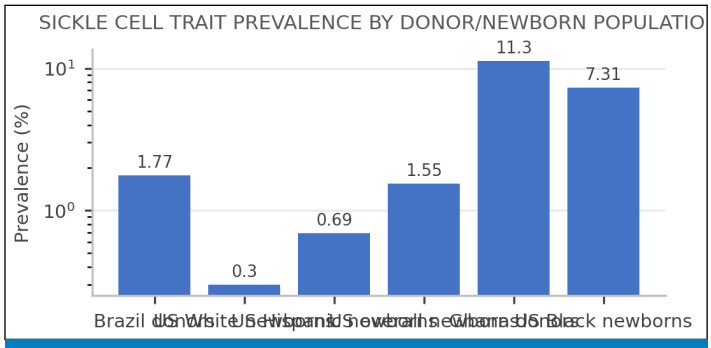

Figure 1: Sickle cell trait prevalence among blood donors and newborns varies widely by population, from 1.77% in a Brazilian donor cohort [6] to 11.3% among donors screened at a Ghanaian teaching hospital [5]; U.S. newborn screening data show a similar spread by race and ethnicity, with 73.1 per 1,000 Black infants versus 3.0 per 1,000 White infants and 6.9 per 1,000 Hispanic infants screening positive in 2010 [7].

United States newborn screening data give the clearest picture of how carrier frequency varies by self-reported race and ethnicity within a single multiethnic health system, and by extension of the pool that will eventually become blood donors. Across 44 states reporting to the CDC in 2010, sickle cell trait was identified in 15.5 per 1,000 screened newborns overall, but the rate was 73.1 per

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1,000 among Black infants, compared with 6.9 per 1,000 among Hispanic infants, 3.0 per 1,000 among White infants, and 2.2 per 1,000 among Asian and Pacific Islander infants; the report estimated more than 60,000 U.S. infants were born with the trait that year [7]. A parallel body of work on Spanish-speaking Latin America has documented substantial but locally heterogeneous HbAS and hemoglobin C carriage tied to regional histories of transatlantic migration, reinforcing that "Hispanic" donors are not a genetically uniform group for hemoglobinopathy purposes [8]. Any urban donor center drawing from several of these communities at once will therefore see a carrier prevalence that sits well above the low single digits typical of a European-ancestry-majority donor base, simply as a function of who walks in the door.

3. Screening approaches used by blood services

Most donor centers have not adopted sickle cell trait screening as a primary, universal test the way they screen for transfusion-transmitted infection. Instead, detection has arrived through three converging routes. The first is legacy sickling-based assays, originally introduced decades ago to flag units whose red cells would not survive standard leukoreduction filtration; sickle-trait-positive units were recognized early as prone to clogging conventional leukocyte-reduction filters, a practical processing problem rather than a donor-health concern, and this is one of the oldest documented reasons blood centers tested donor blood for HbS at all [9]. The second route is molecular: several large donor services now run DNA-based hemoglobinopathy panels, originally built to support antigen-matching and inventory management for patients with sickle cell disease, that incidentally identify carrier donors with high sensitivity and specificity. The third and most consequential shift has been a policy one, exemplified by large donor organizations moving toward proactively testing self-identified Black donors for sickle cell trait and notifying them of the result, both because it can affect an individual's own health decisions and because it changes how their red cells are processed and used.

Table 1: Routes by which blood services detect sickle cell trait in donors, their original purpose, and the reported prevalence findings that motivated them [9,5,6,7,10].

Detection route	Original purpose	Reported carrier prevalence	Downstream handling
Sickling-based assay	Predict leukoreduction filter clogging	11.3% of donors, Ghana [5]	Unit diverted from filtration line
DNA-based hemoglobinopathy panel	Antigen-matching for SCD patients	1.77% of first-time donors, Brazil [6]	Incidental carrier identification
Proactive donor notification	Population-level donor health screening	73.1 per 1,000 Black newborns, U.S. [7]	Donor informed; eligibility unaffected [10]

Whichever route identifies a carrier, downstream handling differs from the interpretation problem facing collectors of units for chronic transfusion or intrauterine use, where sickle-trait-positive red cells are typically diverted away rather than mixed into standard inventory, given theoretical concerns about in vitro cell fragility and diagnostic interference in recipients later tested for hemoglobinopathy. A recent evaluation of donation safety for sickle cell trait carriers found no evidence of an elevated adverse-event rate among these donors during or after standard whole-blood donation, supporting continued donor eligibility while still recommending that centers have a defined process for what happens to the unit and to the donor's own records once a positive result is generated [10].

4. Clinical and exertional risk associated with the trait

The clinical literature that blood centers are, whether they intend to or not, now surfacing for donors is more nuanced than "benign carrier state." The strongest and longest-standing signal concerns exertion under extreme physiological stress. A 1987 study of U.S. Army recruits found that sudden death during basic training occurred at a substantially and significantly higher rate among

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trainees with sickle cell trait than among those without it, a finding that eventually reshaped both military and collegiate athletic screening policy [11,12]. A far larger, more recent cohort of U.S. Army soldiers refined this picture: sickle cell trait carriers had a 54% higher risk of exertional rhabdomyolysis (hazard ratio 1.54, 95% CI 1.12-2.12), comparable in magnitude to the risk conferred by obesity or tobacco use, but no significant excess risk of death from any cause (hazard ratio 0.99, 95% CI 0.46-2.13) [13]. The two studies together argue against framing sickle cell trait as a marker of sudden-death risk in ordinary life, while still supporting real caution around unacclimatized, high-intensity exertion, heat, and dehydration.

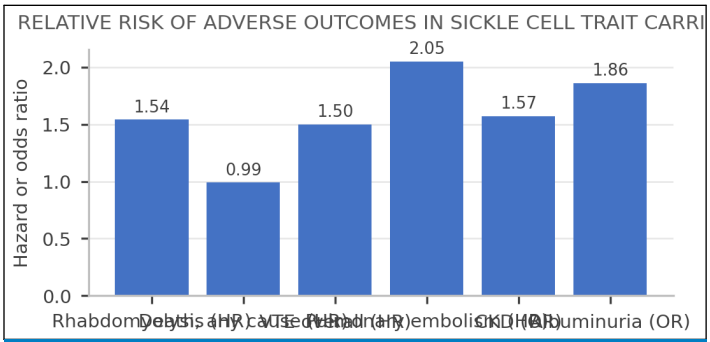

Figure 2: Relative risk estimates for adverse outcomes associated with sickle cell trait, shown as hazard or odds ratios versus non-carriers: exertional rhabdomyolysis (HR 1.54) and all-cause mortality (HR 0.99, not significant) among U.S. Army soldiers [13], venous thromboembolism (HR 1.50) and pulmonary embolism specifically (HR 2.05) in a prospective cohort [14], and chronic kidney disease (OR 1.57) and albuminuria (OR 1.86) in an African American cohort [18].

Away from exercise physiology, population cohorts have linked sickle cell trait to a moderately elevated risk of venous thromboembolism, with a hazard ratio near 1.5 overall and a more pronounced signal for pulmonary embolism specifically (hazard ratio 2.05, 95% CI 1.12-3.76) in a large prospective U.S. cohort [14], alongside evidence of elevated D-dimer levels among trait carriers even without overt thrombosis [15]. A UK primary-care cohort screened for sickle cell trait similarly found an increased incidence of venous thromboembolism relative to matched non-carriers [16], and a systematic review and meta-analysis pooling across the sickle hemoglobinopathy spectrum confirmed the direction of this signal even though its largest effect sizes were concentrated in sickle cell disease rather than trait alone [17]. Renal outcomes show a similar pattern: sickle cell trait was independently associated with chronic kidney disease (odds ratio 1.57, 95% CI 1.34-1.84) and albuminuria (odds ratio 1.86, 95% CI 1.49-2.31) in a large African American cohort [18], a relationship a 2025 systematic review and meta-analysis found to be consistent, if modest, across the accumulated adult cohort literature [19]. At the rarer end of the spectrum sits renal medullary carcinoma, an aggressive malignancy occurring almost exclusively in young people with sickle hemoglobinopathies, first characterized as the "seventh sickle cell nephropathy" and disproportionately affecting carriers of the trait rather than patients with full sickle cell disease [20]. None of these associations individually justifies treating trait carriers as patients, but together they explain why hematologists increasingly resist calling the trait carrier state clinically silent [3].

5. Ethical and notification considerations

Turning a donor screening test into a notification obligation raises questions that blood centers were not originally built to answer. Sickle cell trait status is heritable information with implications for a donor's future reproductive decisions and for biological relatives who were never tested, which places it closer to genetic counseling territory than to a routine infectious-disease result [21]. Because donor screening in many countries has disproportionately identified Black donors, a notification program that targets testing by self-reported race, however well-intentioned, can read as differential surveillance unless it is paired with clear, voluntary opt-in and genuine counseling support rather than a one-line letter [22]. Bioethicists writing on this specific scenario have argued that an incidental finding generated through a donation-related test carries an obligation to notify only when the finding is actionable and when the donor has a reasonable path to follow-up care, criteria that sickle cell

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trait now plausibly meets given the exertional, thrombotic, and renal associations above, but only if the receiving health system has the capacity to provide genetic counseling rather than a diagnosis-and-discharge letter [22,23].

The athletic screening experience is instructive here because it already ran this experiment once, imperfectly. Mandatory NCAA testing of student athletes for sickle cell trait, introduced after wrongful-death litigation rather than as a public-health initiative, was criticized at the time for conflating a legal liability shield with a coherent counseling and disease-management program, and for the reasonable fear that positive results could be used to steer carriers away from competitive opportunities rather than simply to modify training protocols [12]. Donor centers adopting proactive notification have an opportunity to avoid the same trap by decoupling the result from any decision about the donor's continued eligibility to give blood, since the available donation-safety evidence does not support exclusion on the basis of trait status alone [10], and by investing the counseling resources up front rather than after a policy is already in place.

6. Conclusion

Sickle cell trait is common enough in the multiethnic donor pools of large urban blood services that routine or DNA-based hemoglobinopathy testing will keep surfacing it, whether or not a program was designed to look for it. The prevalence literature shows this is not a rare incidental finding in cities with substantial West African, Afro-Caribbean, South Asian, or Latin American donor communities, ranging from just under 2% to more than 11% depending on the population sampled [5,6]. The clinical literature no longer supports calling the trait entirely benign, given consistent associations with exertional rhabdomyolysis, venous thromboembolism, chronic kidney disease, and rare but serious renal malignancy [13,14,18,20], even as the same evidence base is reassuring on the one outcome donors fear most, all-cause mortality. What blood services still lack, in large part, is a shared standard for what happens after a result is generated: a defined counseling pathway, race-neutral eligibility to be tested and informed regardless of self-reported ancestry, and an explicit separation between the donor's clinical result and any judgment about their fitness to continue donating. Building that infrastructure, rather than debating whether to test at all, is the more urgent task now facing transfusion medicine programs in multiethnic urban centers.

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