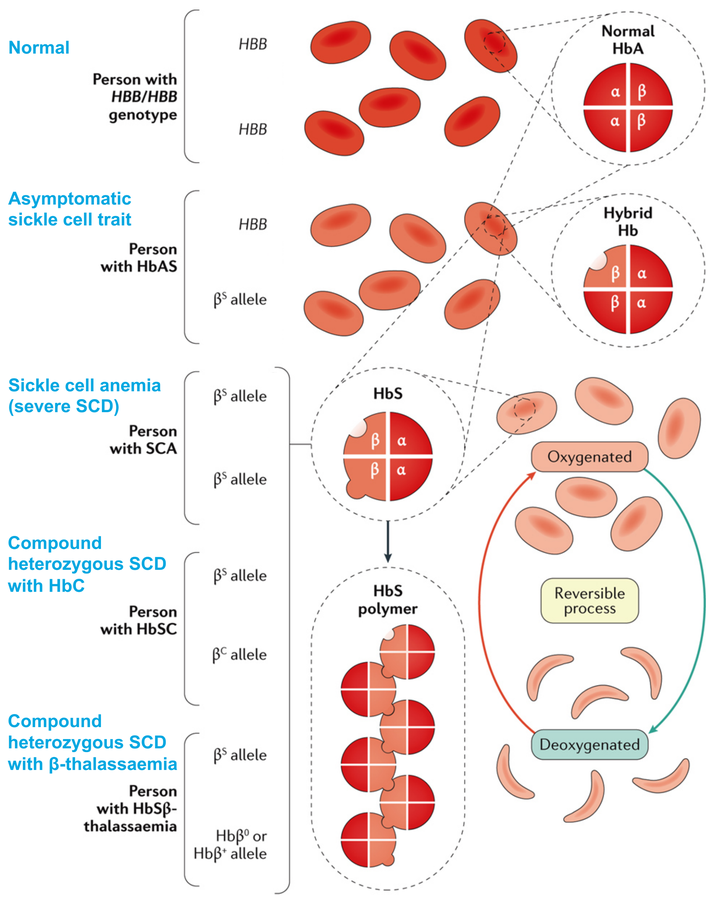
Low-cost screening of sickle cell disease and β-thalassaemia in Nepal

Pranav Shrestha[1], Christopher Bhatla[1], Videsh Kapoor[1], Rajan Pande[2], Boris Stoeber[1]

[1]The University of British Columbia, Vancouver, Canada, [2]Bheri Hospital and Mount Sagarmatha Polyclinic, Nepal

Sickle cell disease (SCD) and β-thalassaemia

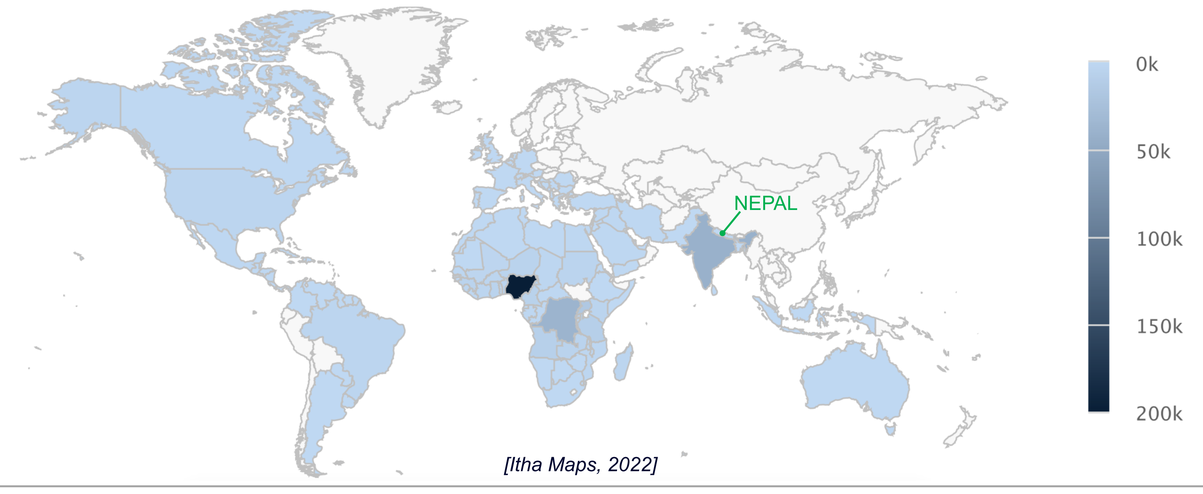


Nature Reviews | Disease Primers

[Figure from G. J. Kato et al. (2018)]

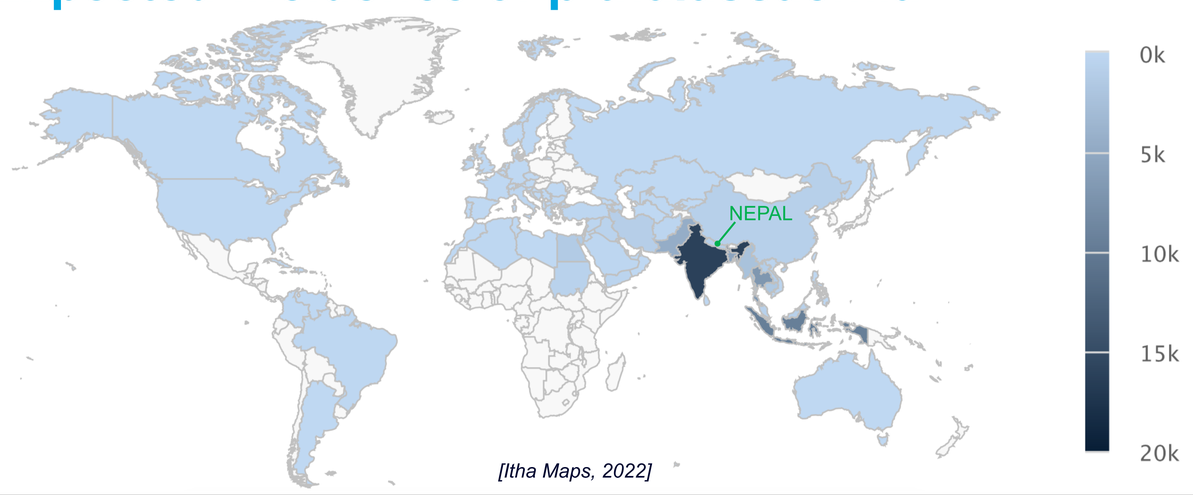
- **Inherited** blood disorders
- **Mutations** in gene encoding hemoglobin subunit **β** (HBB)
- Disease burden for SCD is highest in **low-resource** settings (with childhood mortality between 50-90% [1])
- **Screening** and early diagnosis greatly improves quality of life
- Co-inheritance of HbS and β-thalassaemia can lead to **compound heterozygous** cases
- In countries like **Nepal**, where HbS and β-thalassaemia are both prevalent, it is essential to screen for both
- **Low-cost** and portable options are required to improve screening access in remote and rural settings

Incidence of sickle cell disease



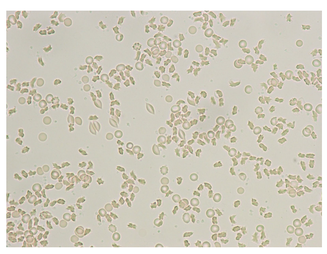
[Itha Maps, 2022]

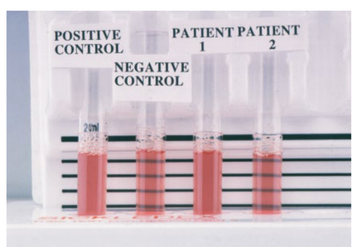
Expected incidence of β-thalassaemia



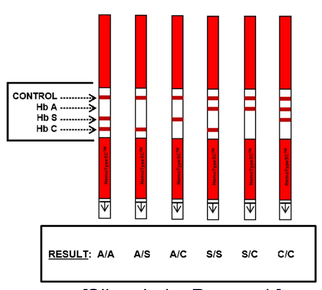
[Itha Maps, 2022]

Screening/diagnostic technologies for sickle cell disease and β-thalassaemia

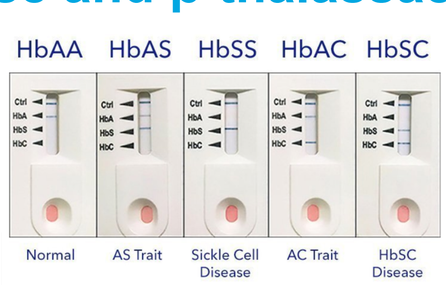




[Figure from B. J. Wild et al., 2017]



[Silver Lake Research]



[BioMedomics Inc.]

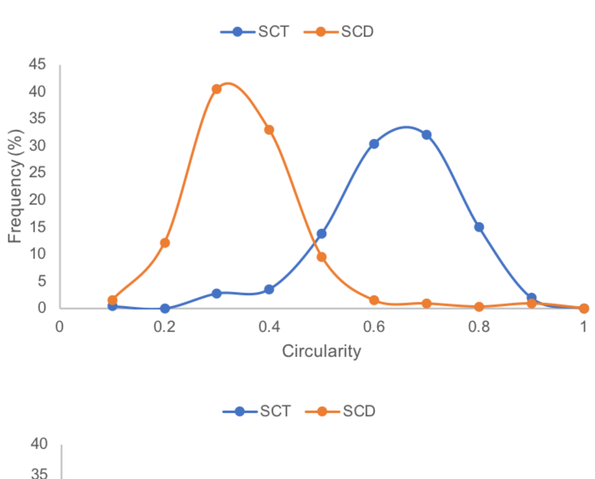
[Hemex Health]

[Bio-Rad Laboratories]

	Sickling test	Solubility test	HemoTypeSC	Sickle SCAN	Gazelle Hb Variant	HPLC
HbS detection	Yes*	Yes*	Yes	Yes	Yes	Yes
β-thal. detection	No	No	No	No	Yes	Yes
Time	30 min – 60 min	5 min	10 min	5 min	8 min	10 min - 60 min
Equipment requiring electricity/battery	Microscope $100 - $2000	None	None	None	Portable reader $1200	Testing unit $10k - $20k
Cost per test	< $1	< $1	$2	$5	$2	$20
Sensitivity	65% - 97.3%	45% - 99%	93.4% - 100%	90% - 100%	100%	Gold standard
Specificity	96% - 99.6%	90% - 99.9%	99.1% - 100%	92.6% - 100%	98%	Gold standard

**Cannot distinguish between SCT & SCD*

Automated sickling test



- **Morphological differences** exist between sickle cell trait (SCT) and SCD in sickling test
- Morphological identifiers:
  - $\boldsymbol{Circularity} = \frac{4 \times \pi \times Area}{Perimeter^2}$
  - $\boldsymbol{Roundness} = \frac{4 \times Area}{\pi \times (Major\ Axis)^2}$
- Traditional sickling test cannot distinguish between SCT and SCD
- **Image analysis** can potentially augment sickling test to distinguish between SCT & SCD
- Can be automated using **machine learning** & **low-cost microscope**

Study plan

Participants

- SCD (HbSS): 20
- SCT (HbAS): 20
- Healthy (HbAA): 20
- HbA/β thalassemia: 20
- HbS/β thalassemia: 20
- Hbβ/β thalassemia: 20

Location: Mount Sagarmatha Polyclinic & Diagnostic Center, Nepalgunj, Nepal

Tests: Automated sickling test, solubility test, HemoTypeSC, Sickle SCAN, Gazelle Hb Variant, HPLC

Planned timeline: Sept, 2022

References

[1] G. J. Kato et al., "Sickle cell disease," *Nat. Rev. Dis. Prim.*, vol. 4, no. 1, p. 18010, Jun. 2018.

[2] B. J. Wild and B. J. Bain, "Investigation of Variant Haemoglobins and Thalassaemias," in *Dacie and Lewis Practical Haematology*, Twelfth Ed., Elsevier, 2017, pp. 282–311.

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MOUNT SAGARMATHA POLYCLINIC & DIAGNOSTIC CENTER, NEPALGUNJ, NEPAL