How to Cite:
Nanda, A. K., Pradhan, S. K., Supakar, S., & Pradhan, P. C. (2022). Prevalence of sickle cell disease among children in India: A systematic review and meta-analysis. *International Journal of Health Sciences*, *6*(S2), 13083–13099.
https://doi.org/10.53730/ijhs.v6nS2.8454

Prevalence of sickle cell disease among children in India: A systematic review and meta-analysis

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***Abstract*---**Sickle Cell Anemia is a common hematological disorder affecting children, mostly from indigenous tribal populations in Africa and India. There is no synthesized evidence to inform policy on its prevalence and distribution across India. Therefore, this systematic review and meta-analysis aims to estimate and summarize the prevalence of Sickle Cell Disease (SCD) and Sickle Cell Trait (SCT) among children aged < 18 years in India. Following standardized methods of systematic reviews, a comprehensive search of all major medical databases was performed. Through independent stepwise screening, ten eligible studies were included in the study. Original peer-reviewed studies reporting the prevalence of either SCD or SCT among Indian children below 18 years of age were included for subsequent methodological quality assessment and data extraction using predefined standardized tools. Random and fixed effects models for meta-analysis were used to arrive at summary estimates for prevalence with 95% confidence intervals. Subgroup analysis was performed among tribal and non-tribal children. The included studies

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.
Manuscript submitted: 09 March 2022, Manuscript revised: 18 April 2022, Accepted for publication: 27 May 2022

used data from around 2 million participants in total. The pooled prevalence of SCD among children in India is 0.8% (95% CI: 0.6-1.0%) and that of SCT was 9.2% (95% CI: 8.5-10.0%). Prevalence of SCD was significantly higher among tribal children at 1.3% (95% CI: 0.8-1.9%) as compared to non-tribal children at 0.4% (95% CI: 0.2-0.6%). The prevalence of SCT was also higher among tribal children at 11.4% (95% CI: 10.2-12.7%) as compared to non-tribal children at 9.2% (95% CI: 8.6-9.9%). India has one of the highest prevalence rates of SCD and SCT among children globally, at 0.8% and 9.2%, respectively. While SCD remains a significant public health challenge in India, the high occurrence of the heterozygous trait increases the chances of future generations having SCD. A significantly higher prevalence of SCD (3-times) and SCT (1.2 times) among tribal children is also reported. SCD is a preventable disease, and a high prevalence in selective population groups that has been shown in this paper needs focused health policy decisions. With improved access to health services, further health systems and policy research is required to initiate and improve the uptake of screening and genetic counseling programs.

***Keywords*---**sickle cell disease, children, systematic review, meta-analysis hematological disorders.

Introduction

Sickle cell anemia is one of the commonest inherited hemoglobinopathies in the world that manifests as Sickle Cell Disease (SCD) and Sickle Cell Trait (SCT) in case of homozygous and heterozygous carriers respectively. (1) The basic pathophysiology of the disease is related to hemoglobin polymerization leading to red blood cell rigidity followed by vaso-occlusion. (1) Around 5% of the world's population are carriers of the sickle cell hemoglobin (HbS) gene, predominantly from the indigenous populations of Africa, India, and Arabia. (2) The burden of SCD/SCT has significant public health implications for these regions, mostly from the global south, and is accentuated by the higher prevalence in marginalized communities such as tribal groups. SCD also contributes significantly to mortality, morbidity, and disability among children. India has one of the highest prevalence of SCD/SCT in the world, second only to African countries.

Around 90% of the cases in Asia are in India and considerable work on sickle cell disease has been done in India but by individual centers and with limited national impact.(3) Within India, generally, a higher prevalence of SCD and SCT has been reported in tribal populations , although with significant variations across groups and geography. (3,4) However, research on SCD in India has been fragmented across scope, regions and disciplines with focus on epidemiological distribution in narrowly selected groups. The lack of nationally representative data on the burden of SCD/SCT, especially among children, is a significant gap in planning public health response against this disorder. (4,5) Additionally, as SCD could be prevented by early screening and pre-marital counselling, it becomes important to

focus a major part of the public health interventions to address SCD among children. (6)

Therefore, a necessary first step is to synthesize available evidence on the burden of SCD/SCT among children in India and identify gaps in research and inform policy decisions for targeted interventions. We carried out a preliminary search of PROSPERO, MEDLINE, the Cochrane Database of Systematic Reviews and the JBI Evidence Synthesis and no current or underway systematic reviews on this topic and context were identified. With this background this systematic review and meta-analysis to estimate and summarize the prevalence of SCD and SCT among children aged < 18 years in India.

Methods

This systematic review was conducted with an *a priori* protocol with no deviations in accordance with the Joanna Briggs Institute methodology for systematic reviews of prevalence and incidence.(7) We used the following selection criteria for the studies:

Participants

All studies that reported the condition of interest among children aged younger than 18 years and carried out in any region of India, in part or exclusively, were included in our review.

Condition

We included studies that reported prevalence of either sickle cell disease or trait or both, diagnosed by any of the standard laboratory tests (such as gel electrophoresis, high performance liquid chromatography etc.), either as part of primary or secondary objectives of the study or even reported as a covariate.

Context

As the focus of the review is to summarize the prevalence of SCD/SCT among children, we have considered only community-based surveys or screening programs in general population/schools/new-borns for our review. We have also excluded studies for which full text was not available/accessible even after contacting authors or for which age classification of participants was not available/reported. For studies presenting duplicate data from same sample, we have included only one of them. We have excluded studies reporting screening in hospital visitors or other high risk groups as these would not provide prevalence estimates in the community. We have also excluded mortality estimates and modelling studies from our review.

Types of studies

Descriptive or analytical observational studies including baseline reports of longitudinal cohort studies and analytical cross-sectional studies were considered for inclusion. Experimental studies and qualitative designs were excluded. We

also excluded conference abstracts or presentations, protocols, books/book chapters, preprints, reviews—narrative or systematic, letters/news articles/opinions/commentaries.

Search strategy

A comprehensive systematic search was performed on January 1, 2022, in the following electronic databases: Medline (via PubMed), Embase (via Ovid), Cochrane CENTRAL library, Proquest, PsycINFO (via Ovid), and CINAHL (via EBSCOHost). In order to keep the search strategy sensitive enough, the databases were searched for those studies that had a mention of the name of India or any of the states in India along with variations of the terms related to SCD/SCT within their abstracts and titles. The detailed search strategy template used is provided in Appendix-1 for MEDLINE. The search strategy, including all identified keywords and index terms, was adapted for each included database and/or information source. The reference list of all included sources of evidence was screened for additional studies.

Study selection

Following the search, all identified citations were collated and uploaded into a reference management software and duplicates were removed. Titles and abstracts were screened by two reviewers independently for assessment against the inclusion criteria. Potentially relevant studies were retrieved in full and their citation details imported into the JBI System for the Unified Management, Assessment and Review of Information (JBI SUMARI) (JBI, Adelaide, Australia).(8) The full text of included articles was assessed in detail against the inclusion criteria by two reviewers. Reasons for exclusion of papers after full-text review that does not meet the inclusion criteria were recorded and reported. The discrepancies were discussed and resolved by consensus. In case of a disagreement, a third author made the decision.

Assessment of methodological quality

Eligible studies were critically appraised by two independent reviewers for methodological quality using standardized critical appraisal instruments from JBI for observational studies.(9) Any disagreements that arose were resolved through discussion. All studies, regardless of the results of their methodological quality, underwent data extraction and synthesis (where possible). Sample size appropriateness was judged by pre-calculated cut offs based on an estimated community prevalence of 1% for SCD and 10% for SCT. (10)

Data extraction

Data were extracted from studies included in the review by two independent reviewers using a modified version of the standardized data extraction tool for prevalence and incidence available in JBI SUMARI. The data extracted included specific details about the condition, populations, study methods, and proportions of interest for SCD/SCT.

Data synthesis

A narrative synthesis of relevant findings from the included studies and the subgroups of interest was done. Studies, where possible, were pooled in a statistical meta-analysis using R software packages (Meta and metafor). (11) Effect sizes were expressed as a proportion with 95% confidence intervals around the summary estimate. Statistical analyses were performed using both random and fixed-effects models using the double arcsine transformation approach. Subgroup analyses were conducted where there was sufficient data to investigate. Heterogeneity was assessed statistically using the standard chi-squared, tau, and I-squared tests. Publication bias was assessed using funnel plots.

Results

Study inclusion

We included a total of 10 articles in this review that were identified from the screening of 14478 articles from database searches and 13 from other sources, mainly citation searching. The details of exclusions and reasons are shown in the PRISMA flow chart below (Figure 1).

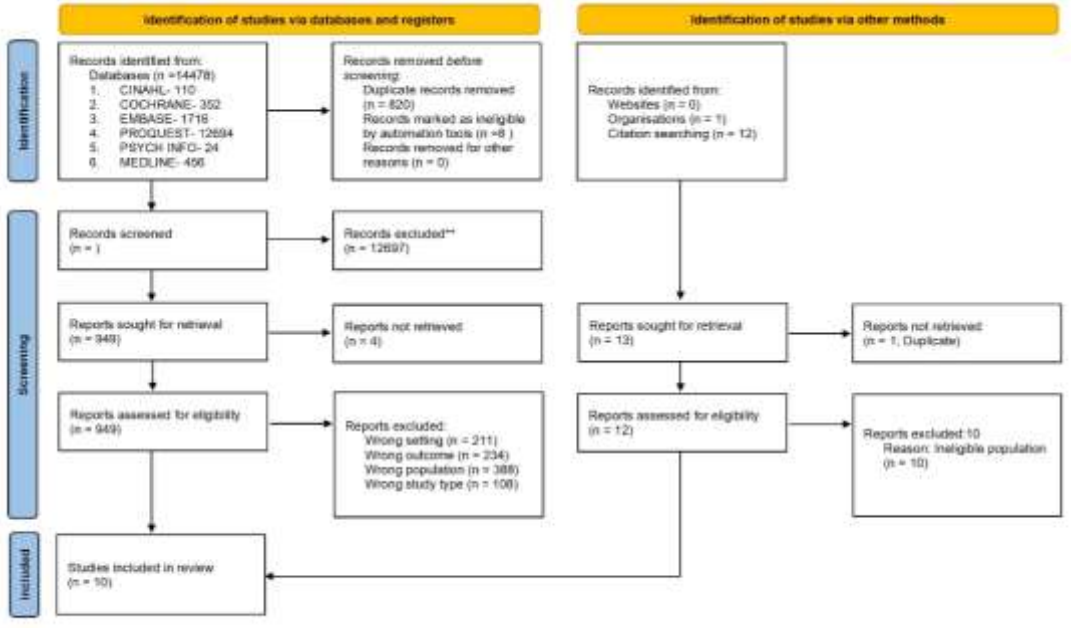

Figure 1. PRISMA flow diagram of the study selection procedure

Methodological quality of the included studies

The methodological quality of the included studies as a whole was adequate based on the results of the critical appraisal. All studies were adequate in terms of the sampling frame and methods used and provided details of study settings, data

analysis, SCD/SCT identification methods, and statistical analysis. While 80% of the studies had an adequate sample size for estimation of SCT, only 2 studies were powered enough for SCD estimations. The details of the critical appraisal findings of the included studies are provided in table 1.

Table-1. Methodological quality assessment of the included studies

Study ID	Appropriate Sample frame	Appropriate Sampling	Adequate Sample size for		Detailed Study setting	Adequate Data analysis	Adequate Methods for SCD/SCT identification	Reliable Measurement of SCD/SCT	Appropriate Statistical analysis	Adequate Response rate
			SCD	SCT						
Chourasia 2020	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
Das 1995	Y	U	N	N	Y	Y	Y	Y	Y	U
Deshmukh 2006	Y	U	N	Y	Y	Y	Y	Y	Y	U
Fareed 2016	Y	U	N	Y	Y	Y	Y (SCT)	Y	Y	U
Italia 2015	Y	Y	N	Y	Y	Y	Y	Y	Y	U
Jain 2012	Y	Y	N	Y	Y	Y	Y	Y	Y	U
Mishra 2019	Y	Y	Y	Y	Y	Y	Y	Y	Y	U
Patra 2011	Y	Y	Y	Y	Y	Y	Y	Y	Y	U
Osmra 2011	Y	Y	N	Y	Y	Y	Y	Y	Y	Y
Teli 2016	Y	Y	N	N	Y	Y	Y	Y	Y	Y
%	100%	70%	20%	80%	100%	100%	100%	100%	100%	30%

Characteristics of included studies

The review synthesized results from around two million children in total collected between 1992 and 2017. It was noted that only seven states in India have reported studies on sickle cell anemia. These are also the states with a large tribal population. The age groups of participants were variable with most studies focussing on school-age children and two studies among newborns. All studies included participants from both genders (no studies reported transgenders or other genders). While four studies reported findings from community-based screenings, two were from newborn screenings and three from school-based screening programs. A lone study was a survey among tribals working in tea gardens. Four studies each relied on gel electrophoresis and high-performance liquid chromatography (HPLC) for the diagnosis of SCD/SCT. One study used both the above methods and one study relied on a slide-based sickling test. The descriptive characteristics of the included studies are summarized in the table-2 below.

Table-2. Summary of descriptive findings from the included studies

Study ID	Year	State	Participant characteristics		Conditions and measurement methods	Description of main results				
			Age groups included-	Setting -		Sample Size	Prevalence of SCD=	Prevalence of SCT=	Gender wise:	Remarks P=Prevalence
Chourasia 2020	2015-17	MP	≤16 years ; (Median=15 years)	Screening among Tribal schools and hostels	Electrophoresis and HPLC	3992	0.7%	14.4%	NA	P of SCD and SCT in tribal children=0.7% and 15.2% respectively; P of SCD and SCT in non-tribal children=0.4% and 16.4% respectively;
Das 1995	1992-93	Odisha, MP, Mah.	8-18 years	Community-based screening in tribal populations	Electrophoresis	336	3.0%	7.1%	P of SCD and SCT in males= 2.3% and 6.8% respectively P of SCD and SCT in females= 6.8% and 9.1% respectively	-
Deshmukh 2006	1996-97	Mah.	≤15 years	Community based screening in rural populations	Electrophoresis	3246	0.1%	2.2%	NA	-
Fareed 2016	2013-14	J&K	6-15 years	Community based survey in 'Muslim households'	Slide examination	676	0.3% (projected)	9.8%	P of SCD and SCT in males= 0.2% and 8.8% respectively P of SCD and SCT in females= 0.3% and 10.8% respectively	-
Italia 2015	2012-14	Gujrat	Newborns	Newborn screening in tribal predominant areas	HPLC	5467	0.6%	12.8%	NA	P of SCT in tribal and non-tribal children=13.8% and 3.3% respectively
Jain 2012	2009-11	Mah.	Newborns	Newborn screening (2-step: mothers screened,	HPLC	8243	1.1%	6.5%	NA	P of SCD in tribal and non-tribal children=1.1% and 1.0% respectively

				followed by babies of those testing positive)						
Mishra 2019	2007-17	CG	3-15 years	School based screening	Electrophoresis	1512801	0.37%	9.9%	NA	P of SCD in tribal and non-tribal children=0.35% and 0.38% respectively; P of SCT in tribal and non-tribal children=9.6% and 9.9% respectively
Patra 2011	2007-10	CG	3-15 years	School based screening	Electrophoresis	359823	0.21%	9.3%	P of SCD and SCT in males= 0.21% and 9.2% respectively P of SCD and SCT in females= 0.21% and 9.4% respectively	P of SCD in tribal and non-tribal children=0.21% and 0.21% respectively; P of SCT in tribal and non-tribal children=9.3% and 9.3% respectively
Qamra 2011	2009-10	MP	≤12 years	Community based survey in tribal population	Electrophoresis	6190	1.6%	11.8%	P of SCT in males and females= 13.3% and 13.6% respectively	-
Teli 2016	2014-15	Assam	<19 years	Survey among tribals working in tea gardens	HPLC	341	12.3%	12.3%	NA	-

MP= Madhya Pradesh, Mah= Maharashtra, CG= Chattisgarh, J&K = Jammu and Kashmir, HPLC= High performance liquid chromatography

Review findings

The pooled prevalence of SCD among children in India is 0.8% (95% CI: 0.6-1.0%). Similarly, the pooled prevalence of SCT among children in India was 9.2% (95% CI: 8.5-10.0%). The forest plots for the meta-analysis is given in the figure-2 below.

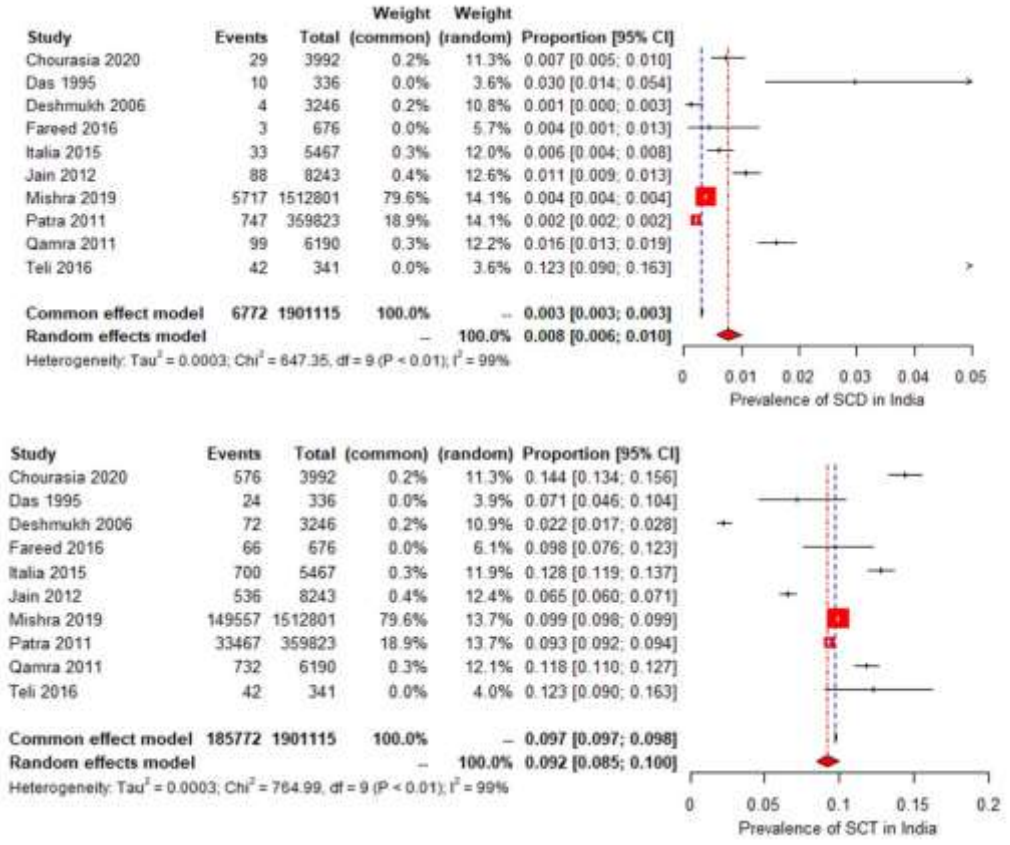

Figure 2. Prevalence of Sickle Cell Disease and Trait among children in India

Prevalence of SCD was significantly higher among tribal children at 1.3% (95% CI: 0.8-1.9%) as compared to non-tribal children at 0.4% (95% CI: 0.2-0.6%). Similarly, the prevalence of SCT was also higher among tribal children at 11.4% (95% CI: 10.2-12.7%) as compared to non-tribal children at 9.2% (95% CI: 8.6-9.9%). The comparisons are shown in the forest plots of the meta-analysis in figures-3 and 4 below.

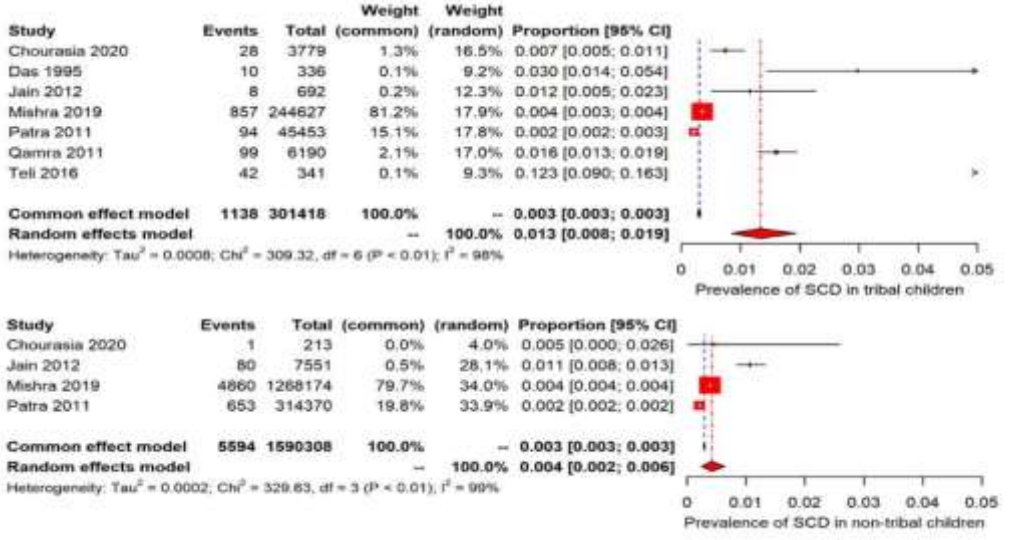

Figure 3. Prevalence of Sickle Cell Disease among tribal and non-tribal children in India

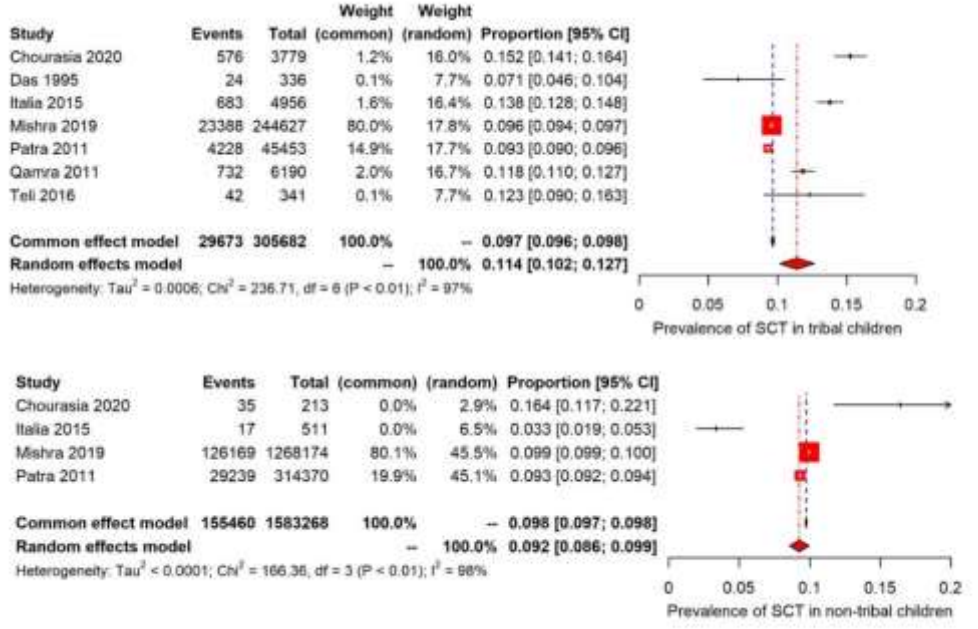

Figure 4. Prevalence of Sickle Cell Trait among tribal and non-tribal children in India

All meta-analyses reported a high degree of heterogeneity in the study results. The funnel plot is given in the figure-5 below.

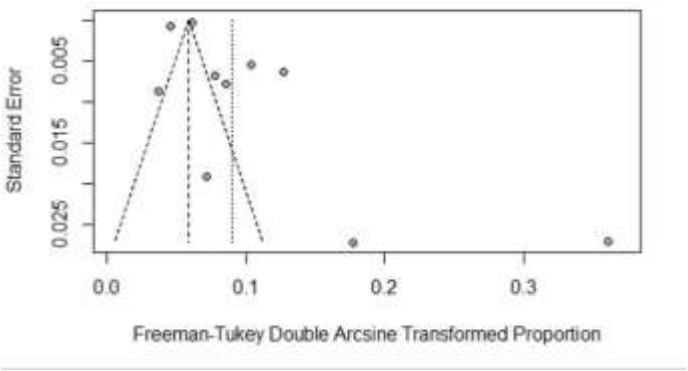

Figure 5. Funnel plot for the included studies

Discussion

This review summarized and synthesised findings from 10 studies from India among children that included of around 2 million participants. The pooled prevalence of SCD and SCT among children in India was 0.8% and 9.2% respectively. Prevalence of SCD and SCT was significantly higher among tribal children as compared to non-tribals. The distribution of the sickle cell hemoglobin gene depends on 2 factors- selective survival advantage of carriers in malaria endemic regions and the second is the migration pattern across the globe.(1)

While the first report on SCD from Southern India was in 1952, considerable variation in carrier frequency has been reported since by individual studies ranging between 1-35%. (3,12) While generally SCD/SCT are considered to be a public health challenge in tribal populations, some states such as Odisha, Chhattisgarh and Madhya Pradesh have reported a higher prevalence of sickle cell trait in non-tribal groups, widening the scope for interventions needed. (3,4) This justifies the need for synthesised data on the prevalence estimates across India. Geospatial modelling estimates based on prevalence data among adults also show that SCD/SCT is more among tribal groups and in central and southern hilly regions that have generally been associated with tribal populations. (10)

While our review considered only peer reviewed published data, a large source of government data generated from screening programs among tribal school children in various states that does not meet the criteria above is also available. This data from over 11 million children reports a significantly lower prevalence of SCD at 0.41% and SCT at 8.33% in tribal children which is similar to non-tribal children. (13) This suggests that the countrywide dissimilarities between tribal and non-tribal groups may not be as significant as the findings from central Indian 'hotspots' may suggest. State wise data is not consistently available and this limits generalizations made for the country from regional studies.

The clinic-epidemiological picture of SCD is unique in India. Electrophoresis and chromatography-based screening and diagnosis tools for SCD are now widely available and relatively inexpensive.(1) Similarly, there is now sufficient evidence

on pharmacological and non-pharmacological interventions for managing Sickle Cell Anemia. (14) There is also substantial literature on the burden of SCD from India and our systematic review provides the necessary synthesis of this.(15) Further implementation research on specific public health interventions is now required to fill gaps in the health system response to this challenge. (5,15,16)

While it is known that new-born screening decreases morbidity and mortality due to SCD in children under 5 years of age, but it is yet to be scaled up in India.(3,4) While new-born screening is well accepted in Indian communities, evidence on antenatal and prenatal screening, which is practiced in some countries, remains uncertain. (1,6) Our review provides information on SCD estimates that will help with resource prioritization for scale-up strategies of screening programs in the country.

In India, priority setting and policy making on SCD has traditionally been under the domain of Ministry of Tribal Affairs as opposed to the Ministry of Health, highlighting the need for inter-departmental coordination. Significant challenges in the national response to this challenge remain, such as lack of a central database or registry and unclear national research priorities. (13) Importantly, central funds released for SCD/SCT screening and management across India has been reduced by over 10-times since 2014-15, while the disease burden has remained same. (13) A focussed agenda for large scale interventions to address SCD, with prioritized resource allocation across vulnerable and high burden groups in India is required in the coming years.

While this review attempts to answer a highly relevant and focused research question, its strengths include a robust methodology, use of standardized tools and a highly sensitive search strategy. It has a few limitations as well. A single study among tribals from Rajasthan was published after the review commenced and was hence not included for in this paper. (17) Another limitation was the high degree of heterogeneity reported in our study. The review has included studies with moderate to good methodological quality. However, variations in populations, settings and other potential bias in individual studies may impact the findings.

Conclusion

Our systematic review that synthesized data from around 2 million participants is the first from India to summarize the prevalence of SCD and SCT. With one of the highest prevalence rates among children in the world at 0.8%, SCD remains a major public health challenge in India. The heterozygous trait is present in over 9% of children increasing the chances of future generations having SCD. Concurrently, anemia in childhood and adolescents remains high as well. We identified a significantly higher prevalence of SCD (3-times) among tribal children. However, prevalence of SCT, although higher in tribal children, was only about 20% greater than non-tribal children.

With improved access to screening services, further implementation research and health systems interventions are required to improve the uptake of these screening and genetic counselling programs. SCD is a preventable disease and a

high prevalence in selective population groups that has been shown in this paper needs focused health policy decisions.

Highlights

- Prevalence of Sickle Cell Disease is high in Indian children (0.8%)
- Prevalence of Sickle Cell Trait is 9.2%
- Higher prevalence of both SCD and SCT is seen in tribal children

Abbreviations- SCD: Sickle Cell Disease, SCT: Sickle Cell Trait

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Appendices
Appendix-A (Search Strategy)
Concept of sickle cell disease

Concept	Mesh	tiab
Sickle cell disease	Anemia, Sickle Cell[mesh] **Sickle Cell Trait[Mesh]** Synonyms: Sickle Cell Anemias; Sickle Cell Disease; Sickling Disorder Due to Hemoglobin S; (Hemoglobin S Disease*); Sickle Cell Diseases; Hemoglobin S Diseases; Cell Diseases, Sickle; Sickle Cell Anemia; Disease, Hemoglobin S; Cell Disorder, Sickle; Anemias, Sickle Cell; Cell Disorders, Sickle; Sickle Cell Disorders; Cell Disease, Sickle; HbS Disease; Sickle Cell Disorder	• Anemias, Sickle Cell • Sickle Cell Anemia* • Sickle Cell Anaemia* • Hemoglobin S Disease • Disease, Hemoglobin S • Hemoglobin S Diseases • Sickle Cell Disorder* • Sickle Cell Disorder • HbS Disease • Cell Disease, Sickle • Cell Diseases, Sickle • Sickle Cell Disease* • **("Sickle cell")** • **("sickle cell trait")** • **("sickle cell trait*")**
India	India(mesh)	• India[TIAB] • Uttar Pradesh[TIAB] • Maharashtra[TIAB] • Karnataka[TIAB] • Kerala[TIAB] • Gujarat[TIAB] • Tamil Nadu[TIAB] • West Bengal[TIAB] • Andhra Pradesh[TIAB] • Rajasthan[TIAB] • Chhattisgarh[TIAB] • Madhya Pradesh[TIAB] • Bihar[TIAB] • Punjab[TIAB] • Assam[TIAB]

		• Odisha[TIAB] • Haryana[TIAB] • Jammu and Kashmir[TIAB] • Telangana[TIAB] • Jharkhand[TIAB] • Goa[TIAB] • Himachal Pradesh[TIAB] • Arunachal Pradesh[TIAB] • Tripura[TIAB] • Nagaland[TIAB] • Sikkim[TIAB] • Mizoram[TIAB] • Manipur[TIAB] • Meghalaya[TIAB] • Uttarakhand[TIAB] • “Andaman & Nicobar Islands”[TIAB] • Chandigarh[TIAB] • “Dadra & Nagar Haveli”[TIAB] • “Daman & Diu”[TIAB] • Delhi[TIAB] • Lakshadweep[TIAB] • Puducherry[TIAB] • Ladakh[TIAB]

Hits : 30,327

((((("Anemia, Sickle Cell"[Mesh] OR "Anemias, Sickle Cell" OR "Sickle Cell Anemias" OR "Hemoglobin S Disease" OR "Disease, Hemoglobin S" OR "Hemoglobin S Diseases" OR "Sickle Cell Anemia" OR "Sickle Cell Disorders" OR "Sickle Cell Disorder" OR "HbS Disease" OR "Sickle Cell Disease" OR "Cell Disease, Sickle" OR "Cell Diseases, Sickle" OR "Sickle Cell Diseases")) OR ("Sickle cell")) OR ("sickle cell trait")) OR (Sickle Cell Trait[Mesh]) OR ("sickle cell trait*")

Hits: 165,279

("India"[Mesh] OR India[TIAB] OR "Uttar Pradesh"[TIAB] OR Maharashtra[TIAB] OR Karnataka[TIAB] OR Kerala[TIAB] OR Gujarat[TIAB] OR "Tamil Nadu"[TIAB] OR "West Bengal"[TIAB] OR "Andhra Pradesh"[TIAB] OR Rajasthan[TIAB] OR Chhattisgarh[TIAB] OR "Madhya Pradesh"[TIAB] OR Bihar[TIAB] OR Punjab[TIAB] OR Assam[TIAB] OR Odisha[TIAB] OR Haryana[TIAB] OR "Jammu and Kashmir"[TIAB] OR Telangana[TIAB] OR Jharkhand[TIAB] OR Goa[TIAB] OR "Himachal Pradesh"[TIAB] OR "Arunachal Pradesh"[TIAB] OR Tripura[TIAB] OR Nagaland[TIAB] OR Sikkim[TIAB] OR Mizoram[TIAB] OR Manipur[TIAB] OR Meghalaya[TIAB] OR Uttarakhand[TIAB] OR "Andaman & Nicobar Islands"[TIAB] OR Chandigarh[TIAB] OR "Dadra & Nagar Haveli"[TIAB] OR "Daman & Diu"[TIAB] OR Delhi[TIAB] OR Lakshadweep[TIAB] OR Puducherry[TIAB] OR Ladakh[TIAB])

13098

Hits: 456
(((((("Anemia, Sickle Cell"[Mesh] OR "Anemias, Sickle Cell" OR "Sickle Cell Anemias" OR "Hemoglobin S Disease" OR "Disease, Hemoglobin S" OR "Hemoglobin S Diseases" OR "Sickle Cell Anemia" OR "Sickle Cell Disorders" OR "Sickle Cell Disorder" OR "HbS Disease" OR "Sickle Cell Disease" OR "Cell Disease, Sickle" OR "Cell Diseases, Sickle" OR "Sickle Cell Diseases")) OR ("Sickle cell")) OR ("sickle cell trait")) OR (Sickle Cell Trait[Mesh]) OR ("sickle cell trait*")) AND (("India"[Mesh] OR India[TIAB] OR "Uttar Pradesh"[TIAB] OR Maharashtra[TIAB] OR Karnataka[TIAB] OR Kerala[TIAB] OR Gujarat[TIAB] OR "Tamil Nadu"[TIAB] OR "West Bengal"[TIAB] OR "Andhra Pradesh"[TIAB] OR Rajasthan[TIAB] OR Chhattisgarh[TIAB] OR "Madhya Pradesh"[TIAB] OR Bihar[TIAB] OR Punjab[TIAB] OR Assam[TIAB] OR Odisha[TIAB] OR Haryana[TIAB] OR "Jammu and Kashmir"[TIAB] OR Telangana[TIAB] OR Jharkhand[TIAB] OR Goa[TIAB] OR "Himachal Pradesh"[TIAB] OR "Arunachal Pradesh"[TIAB] OR Tripura[TIAB] OR Nagaland[TIAB] OR Sikkim[TIAB] OR Mizoram[TIAB] OR Manipur[TIAB] OR Meghalaya[TIAB] OR Uttarakhand[TIAB] OR "Andaman & Nicobar Islands"[TIAB] OR Chandigarh[TIAB] OR "Dadra & Nagar Haveli"[TIAB] OR "Daman & Diu"[TIAB] OR Delhi[TIAB] OR Lakshadweep[TIAB] OR Puducherry[TIAB] OR Ladakh[TIAB]))

Appendix-B (List of included Studies)

1. Patra PK, Chauhan VS, Khodiar PK, Dalla AR, Serjeant GR. Screening for the sickle cell gene in Chhattisgarh state, India: an approach to a major public health problem. J Community Genet. 2011 Sep;2(3):147–51.
2. Italia Y, Krishnamurti L, Mehta V, Raicha B, Italia K, Mehta P, et al. Feasibility of a Newborn Screening and Follow-up Programme for Sickle Cell Disease among South Gujarat (India) Tribal Populations. J Med Screen. 2015 Mar;22(1):1–7.
3. Fareed M, Anwar MA, Ahmad MK, Afzal M. Gene frequency reports of sickle cell trait among six human populations of Jammu and Kashmir, India. Gene Rep. 2016 Sep;4:1–5.
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7. Jain DL, Sarathi V, Upadhye D, Gulhane R, Nadkarni AH, Ghosh K, et al. Newborn Screening Shows a High Incidence of Sickle Cell Anemia in Central India. Hemoglobin. 2012 Aug;36(4):316–22.

8. Mishra H, Neralwar A. Prevalence of Sickle Cell Disease Among School-age Children in Chhattisgarh, India: Predictions, Implications and Interventions. J Health Manag. 2019 Dec;21(4):601–11.
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10. Das MK. Sickle cell gene in Central India: Kinship and geography. Am J Hum Biol. 1995;7(5):565–73.