International Journal of Community Medicine and Public Health
Desai G et al. Int J Community Med Public Health. 2016 May;3(5):1282-1287
http://www.ijcmph.com
pISSN 2394-6032 | eISSN 2394-6040

DOI: http://dx.doi.org/10.18203/2394-6040.ijcmph20161399

Research Article

Initial outcomes of a comprehensive care model for sickle cell disease among a tribal population in rural western India

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Received: 14 March 2016
Accepted: 13 April 2016

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ABSTRACT

Background: Sickle cell disease (SCD) is the most prevalent inherited blood disorder worldwide, and is increasingly recognized as a neglected chronic disease. Several cost-effective interventions have dramatically reduced morbidity and mortality from SCD in developed countries. However, access to care for SCD in India is limited in most rural tribal regions with the highest SCD prevalence.
Methods: In 2014, we implemented a comprehensive care model in rural Gujarat, India, with the aim of providing high-quality screening and treatment to increase coverage of proven interventions for sickle cell disease. Components of the intervention include: new-born, antenatal and family screening; outpatient sickle cell clinic; inpatient protocols; chronic disease registry; and health education. We followed a cohort of patients enrolled between February 2014 and October 2014 and compared the severity of disease and coverage of proven interventions at baseline and after one year of follow-up.
Results: Of 164 patients diagnosed with sickle cell disease who enrolled in the comprehensive care program, 72 patients (43.9%) had SCD pain crises, 59 (35.9%) were hospitalized, 43 (26.2%) received blood transfusions, and 3 (1.8%) died during follow-up. Compared to baseline, coverage of pneumococcal vaccine (0.6% to 78.5%, p<0.001) and hydroxyurea (4.5% to 50.0%, p=0.002) significantly improved. There was a reduction in the proportion of patients with ≥3 pain crises per year (35.4% to 9.8%, p<0.001) and the proportion of patients with ≥1 hospitalization per year (56.7 go 36.0%, p<0.001) with no significant change in patients with ≥1 blood transfusion in last year (32.9% to 26.2%, p=0.127).
Conclusions: This study demonstrates that implementing a continuity care model for sickle cell disease in rural India is feasible and can improve coverage of evidence-based interventions.

Keywords: SCD, Comprehensive care model, Coverage of proven interventions, Tribal, Rural

INTRODUCTION

Sickle cell disease (SCD) is the most prevalent inherited blood disorder worldwide, characterized by sickling of red blood cells leading to complications due to vaso-occlusion and anemia.[1] Sickle cell disease represents a major public health problem in India where 15% of the world's neonates with SCD are born every year.[2,3] Within India, the prevalence of sickle cell trait is highest among tribal populations, varying from 1-40%.[4-6] An estimated 18 million Indians have sickle cell trait and.[1] 4 million have sickle cell disease.[7] Several studies have found

severe disease manifestations in 20-50% of Indian SCD populations, the majority presenting with severe anemia, acute febrile illnesses, and frequent vaso-occlusive crises.[8-10]

Several simple, cost-effective interventions have dramatically reduced morbidity and mortality from sickle cell disease in developed countries, including: early diagnosis by neonatal screening, preventive care with prophylactic penicillin and pneumococcal vaccination, and regular follow-up and treatment with transfusion and hydroxyurea for severe cases.[11-14] These interventions proven to improve SCD outcomes have not been well-studied in Indian populations.

Access to care for sickle cell disease is limited in India, especially among tribal communities that bear the highest burden of disease.[3-4,15] There has been recent interest from the Indian government to further develop sickle cell disease programs in high prevalence areas. The state of Gujarat was the first state in India to implement a sickle cell anemia control program in 2006.[7] With statewide screening methods, more patients with SCD are diagnosed, but limited infrastructure exists to ensure that treatment and prevention reach these vulnerable populations. There is a need to find and document effective programmatic strategies to increase coverage of proven interventions. We describe here initial outcomes of a comprehensive sickle cell program implemented among a resource-limited tribal population in rural south Gujarat, India with the aim of providing high-quality comprehensive screening and treatment to increase coverage of proven interventions among individuals with sickle cell disease.

METHODS

Study setting and program description

SEWA rural is a non-profit health and development organization based in rural Jhagadia, South Gujarat, India. Since 1980, SEWA rural has operated a comprehensive local health delivery system, consisting of a 150 bed sub district hospital, outpatient clinics, and a robust community healthcare worker outreach program. SEWA rural serves a catchment area of approximately 1500 villages with a population of 1,500,000.[16] The majority of the population is from tribal communities, largely subsistence farmers earning less than the international poverty line.[17] Local epidemiological data suggests that the prevalence of sickle cell trait in the population seeking care at SEWA Rural hospital is approximately 15% and sickle cell disease 2%.

In 2014, we implemented a multifaceted sickle cell program at SEWA rural to provide continuity of care to patients with sickle cell disease. The comprehensive care model includes screening, standardized outpatient and inpatient protocols, population management, and health education components (Figure 1). All pregnant women, newborns of mothers with sickle cell trait or disease, family members of patients with sickle cell disease, and patients with anemia or symptoms of sickle cell disease who are seen in the SEWA rural health care system are provided screening. Any patient who screens positive for sickle cell disease are offered enrollment in the sickle cell disease registry, provided with health education and counseling, and scheduled for outpatient care in the sickle cell clinic.

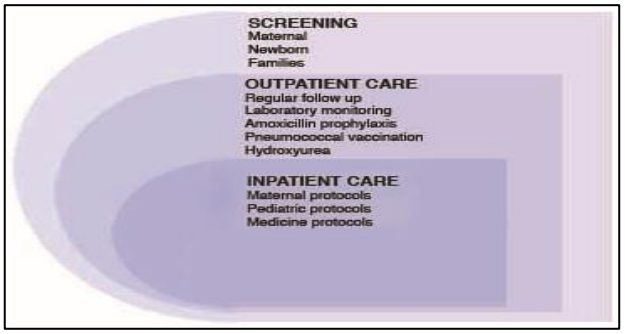

Figure 1: Program description.

Table 1: Description of outpatient clinical interventions.

Clinical intervention	Age	Frequency
PCV 23 vaccine	>2 years	Once
PCV13 vaccine	2 month, 4 month, 6 month, 15 month	4 doses
Amoxicillin prophylaxis	2 month -5 years	Daily
Folic acid	all ages	Daily
Hydroxyurea	>9 month if indicated	Daily
CBC	all ages	Q3 month, Q1 month if on Hydroxyurea
Liver and kidney function tests	all ages	Q12 month, Q3 month if on Hydroxyurea

The outpatient sickle cell clinic serves as the medical home for these patients. The clinic is staffed by a physician and clinical social worker, who provide sickle cell counseling and treatment services. Patients are scheduled for outpatient clinic visits every three months, where they receive laboratory monitoring, preventive and chronic disease care as recommended by national and international guidelines (Table 1).[18-19] Patients receive pneumococcal vaccination, folic acid supplementation, and patients under age five receive amoxicillin prophylaxis. Hydroxyurea is prescribed for those patients who have any of the following in the previous year: ≥3 pain crises, ≥hospitalizations, ≥3 blood transfusions or a history of acute chest syndrome, splenic sequestration

crisis, and avascular necrosis of the bone or ischemic stroke.

All identified patients are also entered into the SCD registry, which includes information on demographics, disease history, laboratory results, clinic visits, treatment, complications, transfusions, hospital admissions, and mortality. The registry is used for proactive panel management to follow quality metrics for performance improvement, and conduct outreach to patients overdue for routine visits and monitoring. The sickle cell counselor contacts patients via phone who are overdue for follow-up.

Patient population and selection of participants

All patients within the SEWA rural health care system that were diagnosed with SCD between February 2014 and October 2014 and enrolled in the comprehensive sickle cell program were included in this analysis. Most of these patients were diagnosed with SCD during a hospitalization or routine screening. Follow-up data over one year was included for each patient.

Measurements

Initial screening for sickle cell disease was conducted with the sand sickling test.[20] Any positive tests were confirmed with hemoglobin electrophoresis by high-performance liquid chromatography (HPLC). Newborn screening was conducted by dried heel prick blood spots tested by HPLC using the newborn screening machine (Bio-rad laboratories, Hercules, CA) according to manufacturer instructions. During enrollment, patient self-report of prior pain crises, the number of hospitalizations, and the number of blood transfusions in the year prior to enrollment were recorded. Baseline laboratory testing included complete blood count, creatinine, liver function tests, and hemoglobin electrophoresis. During one year of follow-up, complete blood count was measured every three months, and creatinine and liver function testing annually. Pain crises, receipt of medications, vaccinations, and blood transfusions were recorded during each clinic visit. Hospitalizations within the healthcare system during follow-up were recorded with primary diagnosis and length of stay. Deaths at the hospital or at home that were ascertained during counselor outreach phone calls were recorded.

Statistical analysis

We used the McNemar test/Marginal homogeneity test to compare the measured coverage of proven intervention and impact of intervention between baseline and at 1 year of follow-up. STATA-12 and MS excel 2007 was used to perform this analysis. This program was implemented as a quality improvement project and deemed to be exempt from institutional review board.

RESULTS

Of 7832 patients screened for SCD in 2014, 182 patients were diagnosed with SCD. Of the 182 diagnosed SCD patients, 18 patients (9.8%) did not engage in care after initial diagnosis and were excluded from analysis. 164 patients were enrolled in the comprehensive sickle cell program and followed for one year. Out of 164 patients, 101(61.5%) were female and mean age at enrollment was 18 years. All enrolled patients were from local tribal communities (100% scheduled tribe (ST) caste) (Table 2).

Baseline hemoglobin (Hgb) for our population ranged between 4-12 g/dl with a mean of 8.0 g/dl. There was a significant burden of self-reported pain crises with 38% of patients having 1-2 pain crises and 35.4% of patients having 3 or more pain crises during the year prior to enrollment. Similarly, over the previous year, 56.7% of patients reported at least one hospitalization and 32.9% of patients reported receiving at least one blood transfusion. Prior to enrollment in the comprehensive sickle cell program, few patients had received guideline-recommended treatment. No patients under age five were on penicillin or amoxicillin prophylaxis. Only one patient (0.6%) had received the pneumococcal vaccine, and one patient was on hydroxyurea (0.6%) prior to enrollment.

Table 2: Baseline characteristics and follow-up of participants (n=164).

Characteristic	Frequency (% of total population)
Gender	
Male	63 (38.5%)
Female	101 (61.5%)
Caste	
Scheduled Tribe	164 (100%)
Age	
0-5 years	17 (10.3%)
6-20 years	57 (34.7%)
21-40 years	87 (53%)
41+ years	5 (3%)
Laboratory findings	
Mean Hgb (gm/dl)	8.0
Mean Hgb F (%)	15.6%
Mean Hgb S (%)	70%
Clinic follow-up over 12 months	
O visits	19 (11.6%)
At least 1 visit	145 (88.4%)
At least 2 visits	73 (44.5%)

During 12 months of follow-up after enrollment, 145 patients (88.4%) presented for at least one follow-up clinic visit and 73 patients (44.5%) had at least two visits. 19 patients (11.6%) did not follow-up for any clinic visits after enrollment. During the 12 months of follow-up, 56 patients (34.1%) reported one or two pain crises and 16

patients (9.8%) had 3 or more crises. 59 patients (36.0%) were hospitalized at least once and 43 patients (26.2%) received a blood transfusion. 129 patients (78.7%) received pneumococcal vaccination and 145 patients (88.4%) received folic acid supplementation. Of 17 patients under age five, 4 (23.5%) were taking amoxicillin prophylaxis at 12 months follow-up. Of the 22 patients who met criteria for hydroxyurea, 11 patients (50.0%) were taking hydroxyurea at 12 months follow up.

Compared to baseline, coverage of pneumococcal vaccine ($p<0.001$) and hydroxyurea ($p=0.002$) were significantly improved. There was a reduction in the number of pain crises per year ($p<0.001$) and the proportion of patients with ≥1 hospitalization per year ($p<0.001$). There was no significant change in patients with ≥ 1 blood transfusion in last year ($p=0.125$) (Table 3).

Table 3: Coverage of interventions and sickle cell disease severity at baseline and end line.

Characteristic	Frequency (% of total population) at baseline (n=164)	Frequency (% of total population) at end line (n=164)	p-value
Severity of disease pain crises within past year			
No crises	44 (26.8%)	92 (56.1%)	<0.001
1-2 crises	62 (37.8%)	56 (34.1 %)	0.127
3 or more crisis	58 (35.4%)	16 (9.8%)	<0.001
≥1 blood transfusion in past year	54 (32.9%)	43 (26.2%)	
≥1 hospitalization in past year	93 (56.7%)	59 (36.0%)	
Taking hydroxyurea of those who met criteria (N=22)	1 (4.5%)	11(50.0%)	0.002
Received pneumococcal vaccination	1 (0.6%)	129 (78.7%)	<0.001
Taking penicillin or amoxicillin prophylaxis (age <5, N=17)	0 (0%)	4 (23.5%)	0.125

DISCUSSION

Coverage of proven interventions for sickle cell disease remains limited in many in resource-poor settings.[3,4,15] This study demonstrates the feasibility of implementing a hospital-based comprehensive sickle cell program in a remote rural tribal area of India. The comprehensive sickle cell program met the major SCD quality of care indicators with the majority of patients enrolled in the program receiving the planned interventions.[19] 79% of patients were vaccinated for pneumococcus, which was a marked improvement from the baseline vaccination rate of 0.6%.

It has been previously noted that the sickle cell disease phenotype is more mild in India than the African phenotype.[4,21] However, we found a high prevalence of pain crises, hospitalizations, and blood transfusions among the patient population, indicating that there is a spectrum of disease severity with a significant proportion of patients with sickle cell disease in this tribal region of south Gujarat having serious disease manifestations. We observed a significant reduction in pain crisis and hospitalizations after enrollment in care, though a causal association cannot be determined by the pre-post study design.

Of note, loss to follow-up was a significant issue among the patient population. Our program evaluation demonstrated a step-wise drop off in clinic follow-up rates, which led to decreased coverage of some interventions. 20% of patients did not follow-up for any clinic visits after enrollment, and only 45% of patients had two or more outpatient sickle cell clinic visits. Despite attempted telephone outreach to improve clinic appointment attendance, many patients could not be reached due to inaccurate and frequently changing phone numbers. Further investigation is needed to understand barriers and facilitators of follow-up and identify strategies to improve retention in care for patients with sickle cell disease in rural India.

Limitations of this study include variability in data entry in the paper medical record and disease registry. Coverage of interventions such as pneumococcal vaccination, folic acid supplementation, and amoxicillin and hydroxyurea prescription may have been higher than documented. The program has subsequently switched to an electronic medical record and registry to improve care delivery and documentation. Moreover, some outcomes, such as pain crises at home, are self-reported and subject to recall bias. In addition, the lack of a control group limits causal interpretations of outcomes such as change

in hospitalizations. Future investigation will include use of validated pain and quality of life scales and prospective comparison group.

CONCLUSION

In conclusion, this program demonstrates that implementing a continuity of care model in rural India can significantly improve coverage of evidence-based interventions for treating sickle cell disease. Longer-term prospective evaluation is necessary to assess the clinical efficacy of this delivery model, including its effect on morbidity and mortality. In addition, further investigation is needed to identify strategies to improve retention in care. This rural comprehensive sickle cell program can serve as a model for program development in other resource-limited settings to improve access to care for patients with sickle cell disease.

ACKNOWLEDGEMENTS

We thank the community of Jhagadia and our patients for giving us the opportunity to deliver health services to them. This project was made possible through donations from various donors including the Government of Gujarat and Anupam Rasayan India Ltd. The authors express their gratitude to the Valsad Raktadan Kendra for providing newborn screening services. The authors would also like to acknowledge the SEWA Rural hospital staff members, counselors, doctors, nurses and laboratory staff for implementing this program with great enthusiasm. The authors thank Mr. Ankit Anand for his role towards statistical analysis.

Funding: Government of Gujarat and Anupam Rasayan India Ltd
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Desai G, Dave KK, Banerjee S, Babaria P, Gupta R. Initial outcomes of a comprehensive care model for sickle cell disease among a tribal population in rural western India. Int J Community Med Public Health 2016;3:1282-7.