Effectiveness of a Hospital-based Comprehensive Sickle Cell Care Program to Improve Coverage of Proven Interventions in Tribal Areas of Western India

Kapilkumar Dave, Gayatri Desai[1], Reena Gupta[2], Dhiren Modi, Shrey Desai

Department of Community Health Project, SEWA Rural, [1]Kasturba Hospital, SEWA Rural, Jhagadia, Gujarat, India, [2]Division of General Internal Medicine, San Francisco General Hospital, University of California, San Francisco, California, USA

Abstract

Objective: The objective of this study was to assess the effectiveness of a comprehensive hospital-based sickle cell disease (SCD) model involving improvements of proven interventions in a tribal area of Gujarat, India. **Methods:** This was a quasi-experimental study involving five primary health centers each in the intervention and control groups. This study was conducted from June 2016 to May 2018 in three tribal areas of Gujarat, India. The intervention was a hospital-based comprehensive care model for SCD patients. We included all SCD patients between the ages of 5 and 40 years in the study area. We measured outcomes at baseline and end line by household survey. The analysis was done using a difference-in-difference method. **Results:** A total of 84 and 101 patients were recruited in the intervention and control groups, respectively. The baseline characteristics were comparable in both the groups. At end line, there was a significant difference in coverage of proven interventions including pneumococcal vaccination- odds ratio (OR) 21.3 (95% CI 9.7–46.8, *P* value 0.002), folic acid - OR 4.1 (CI 2.2–7.8, *P* <0.001), chloroquine –OR 4.9 (CI 2.4–10.2, *P* <0.001), and hydroxyurea for severe SCD patients - OR7.1 (CI 1.8–28.6, *P* < 0.001) in the intervention group compared to the control group. The improvement for the clinical outcome indicators including pain crisis rate (mean difference [MD]: −0.18 [−1.17–0.812]), hospitalization rate (MD: −0.08 [−0.375–0.210]), and blood transfusion rate (MD: −0.60 [−0.532–0.412]) in the intervention group in comparison with the control group was nonsignificant. **Conclusion:** This study shows that the comprehensive hospital-based SCD model has great potential to improve the coverage of proven interventions for SCD. Further investigation is needed to assess the impact on clinical outcomes.

Keywords: Hospital-based care model, sickle cell disease, sickle cell disease program, tribal population

Introduction

Sickle cell disease (SCD) is a hereditary genetic disorder of hemoglobin that causes red blood cells to sickle at low oxygen levels.[1] Unlike healthy red blood cells, sickle-shaped red blood cells stack up and cause vaso-occlusion. SCD patients suffer from various symptoms from early childhood, including vaso-occlusive crises, recurrent infections, organ failure, anemia, and stroke. The mortality rate is higher in SCD patients compared to the rest of the population.[2,3]

SCD is prevalent worldwide but has a high prevalence in African countries, South America, Saudi Arabia, and India.[1] In India, SCD prevalence is higher among the tribal populations than the general population. The prevalence of the sickle cell trait is about 5%–34% among the tribal people in India.[4-6] The prevalence of SCD is 0.6%–35% in various areas of Gujarat.[7]

In general, the belief was that affected individuals in India have a milder manifestation of disease than African and Arabian SCD individuals. However, recent studies have found severe manifestations of SCD in 20%–50% of Indian SCD-affected individuals.[8] Several cost-effective, proven interventions are

Access this article online

Quick Response Code:

Website: https://journals.lww.com/jihs

DOI: 10.4103/jihs.jihs_9_23

Address for correspondence: Dr. Kapilkumar Dave, Department of Community Health Project, SEWA Rural, Jhagadia, Gujarat, India.
E-mail: kapil.dave88@gmail.com

How to cite this article: Dave K, Desai G, Gupta R, Modi D, Desai S. Effectiveness of a hospital-based comprehensive sickle cell care program to improve coverage of proven interventions in tribal areas of western India. J Integr Health Sci 2023;11:14-23.

Received: 22-Mar-2023 **Revised:** 31-May-2023 **Accepted:** 10-Jun-2023 **Available Online:** 03-Oct-2023

known to improve outcomes for SCD, including early diagnosis via neonatal screening, education, and counseling of SCD patients and families about early recognition of complications, pneumococcal vaccination, and regular follow-up and treatment with transfusion and hydroxyurea (HU) for severe SCD cases.[9-11] These interventions have been introduced and were found to be effective in Western countries but have not been studied well in India.[12]

In the year 2011, the state government of Gujarat implemented a SCD control program. Screening for SCD among tribal population is completed, although the coverage of the above-proven interventions was found below par in SCD patients in Gujarat.[13] To develop a programmatic strategy to improve the coverage of proven interventions for SCD patients, SEWA Rural developed a hospital-based comprehensive care program for SCD in the tribal area of Gujarat, India.[14] This study aimed to examine the effectiveness of a comprehensive SCD program in community settings.

Methods

Study design and study setting

The study design was a quasi-experimental study involving five primary health centers (PHCs) each in the intervention and control groups. The study was conducted from June 2016 to May 2018 in three tribal blocks of Narmada and Bharuch districts in Gujarat, India.

This study was implemented in Kasturba Hospital managed by SEWA Rural Trust, which is based in the tribal area of Gujarat, India.

Participants

The study was implemented in 10 PHCs in three blocks of Narmada and Bharuch districts that are within a 10–40-km range of Kasturba Hospital. PHCs were assigned randomly into intervention and control groups.

As screening for SCD has been done by government, district health society is supposed to have a list of SCD patients. The list of total 716 patients was received from district health society for these 10 PHCs. It was decided to stop recruitment and interview of new patients once we reach the sample size. Therefore, every participant or group did not have an equal chance of selection. Hence, we called this study a quasi-experimental study.

Initially for a few samples, we did high-performance liquid chromatography (HPLC) of some samples to see the accuracy of data, we found discrepancies in result. Hence, it was decided to do HPLC of all participants before enrollment. All SCD patients aged between 5 and 40 years in the study area were included. Pregnant women were excluded from the study due to confounding complications with pregnancy and delivery.

At baseline, a data collector visited the household of each participant on the list. HPLC was done for all patients to confirm the diagnosis of SCD. Only participants positive for SCD through HPLC were included in the study. The participants from the intervention area were invited to visit Kasturba Hospital for registration. In the intervention group, we included those patients who visited the hospital at least once and registered themselves in SEWA Rural's SCD registry. The data collector visited each household at least three times for those found absent on the first visit. Patients who were not contacted after three home visits were not included in the study.

Intervention

The intervention was comprehensive care program at secondary care hospital. The comprehensive care program for SCD consisted of a weekly SCD clinic, inpatient care, and a web-based IT application as a job aid for doctors and counselors. All SCD patients in the intervention group were enrolled in the IT-based system at Kasturba Hospital. During registration, all patients received health education by a trained counselor about adherence to care, how to prevent pain crisis, when and where to seek care and family screening for SCD. All registered patients followed up once every 3 months at the weekly outpatient clinic. Follow-up care consisted of self-care counseling, laboratory tests, diagnostics, and medical care by qualified health-care workers. Patients received pneumococcal 23 vaccine, folic acid, chloroquine (CHQ), and, in severe cases, HU medicine at every follow-up visit. Emergency medical care and inpatient services, including blood transfusion services, were available at the hospital [Figure 1].

All patients were supposed to revisit the clinic at every 3 months. All visits were recorded in the web-based IT system by a counselor. The web application helps to ensure adherence to care by tracking missing visits. The app generates alerts for the counselor and doctors, which displays names of the patients who missed their respective clinic visits. The counselor made follow-up telephone calls to remind patients about a follow-up appointment. Those patients who did not visit the SCD clinic for 6 months despite phone call follow-ups were marked as lost to follow-up by the counselor. Program managers monitored

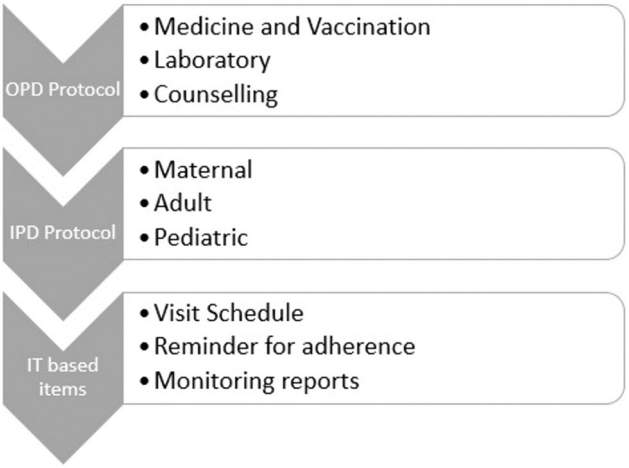

Figure 1: Program description of hospital-based comprehensive sickle cell disease care program

the reports generated by the application in monthly monitoring meetings with programmatic staff. At hospital, doctors followed care protocol based on the recent evidence.[15] Local doctors including gynecologists, pediatricians, and physicians approved the protocol and agreed to follow the protocol for the care.

Control group

The participants in the control arm received the usual care in the government system. As per government system, there is a sickle cell counselor for each PHC. Sickle cell counsellors working at PHCs supposed to visit respective villages to provide home care services including medication and counselling to SCD patients. Pneumococcal vaccination and HU treatment are available at PHC. Although, the laboratory tests including liver profile, complete blood count, kidney profile, and serum bilirubin facilities are not available at PHC. Patients need to travel to district hospital or community health center to avail those reports. A medical doctor is available at PHC, and the blood transfusion facility is not available at PHC. PHCs are suffered due to recurrent medicine short supply. We did not invite participants from the control group for hospital care [Table 1]. As we are only public hospital available in the area, we did not deny care services to people from control area.

Outcomes

The study outcomes include coverage of various proven interventions and severity of disease at baseline and end line.

The primary outcomes of interest were as follows:

1. Pain crisis rate in the past year
2. Proportion of patients with severe SCD who were prescribed and had taken HU at least once within the last week.

The secondary outcome indicators include knowledge of patients about SCD, quality of life (QoL) of the patient, and coverage of pneumococcal 23V vaccine, folic acid, and CHQ.

Definition of outcome variables

Pain crisis is defined differently in various studies.[16-18] Hence, for this study, pain crisis was defined as severe pain in bones, back, or abdomen that limits a patient's routine work and remains for at least 24 h, or sought care from a doctor for pain. The hospitalization was counted when a patient was admitted to any hospital for at least 24 h due to causes related to SCD.

Measurement of outcomes

All outcomes were measured at baseline and end line by interviewing participants by home visit. The severity due to SCD was measured at baseline and end line. At baseline, severity was measured from responses of the baseline survey. To measure the prospective severity of the disease, we made phone calls to all registered patients from both the groups. The phone calls were done every 5–6 months, and patients were asked about crises, hospitalizations, and blood transfusions. This method was validated by comparing it with on-field data collection. If the patient has at least three crises, three hospitalizations, or three blood transfusions due to SCD within 12 months either from phone calls or end line survey, the respective patient was marked as severe SCD. We also asked about the history of complications arising from SCD, including splenic sequestration, stroke, acute chest syndrome, and avascular necrosis of hip due to SCD at baseline and end line survey.

QoL was assessed using a modified questionnaire from the 36-Item Short Form Survey questionnaire[19] and the WHO QOL-Brief questionnaire for QoL.[20] We translated and validated the questionnaire before using it for the survey. The piloting of Gujarati questionnaire was done in the presence of an expert, and the expert confirmed the local language questions being asked as mentioned in the English questionnaire.

A separate team of trained data collectors did a home visit for each participant. The same data collection tool was used at baseline, end line household survey, and phone call follow-up. All data at baseline were collected using a paper-based system, and offline software was developed and used for data entry. End line data collection was done after 2 years. A research associate and statistician monitored the quality of data collection.

Sample size calculation

The sample size was calculated for comparison of two

Table 1: The care provision for the intervention and control groups enrolled under the study of hospital-based comprehensive sickle cell disease program in tribal area of Gujarat, India, 2016–18

	Intervention group	Control group	Note
Government services			
Government counselor services for SCD	√	√	
SCD care at PHC	√	√	
Laboratory testing at district hospital	√	√	
SEWA Rural Hospital-based comprehensive care for SCD			Members of the control group can walk-in and can receive all services from SEWA Rural, but we invited only members of the intervention group
Weekly clinic care	√√	√	
Inpatient care	√√	√	
Laboratory services	√√	√	
Registration to SCD registry	√√	√	

√: The particular group members can avail the services, √√: The particular group members invited and registered to SCD registry of program. SCD: Sickle cell disease, PHC: Primary health center, SEWA: Society for Education Welfare and Action

proportions (two-sided) for primary indicators which are (a) pain crisis rate and (b) number and percent of eligible patients who were prescribed and had taken HU at least once within the last week. As per our previous experience, we expected the crisis rate at end line in the intervention group to be 1.9 crisis/person year as compared to 2.47 crisis/person year in the control group. Similarly, for HU, we expected that 10% of those eligible would receive HU in the intervention group as compared to 1% in the control group. We used $n = (z\alpha/2 + z\beta/2)^2 \times (\pi_1 [1-\pi_1] + \pi_2 [1-\pi_2])/[\pi_1-\pi_2]^2$ formula:[21-23] n = the sample size required in each group (double this for total sample), π_1 = first proportion, π_2 = second proportion, $\pi_1-\pi_2$ = size of difference of clinical importance, and $z\alpha^2$ depends on desired significance level = 1.96. As per the above calculations, the sample size includes 96 cases per group.

Statistical analysis plan

Intention-to-treat analysis was performed for all outcomes. Baseline characteristics were examined by *t*-test for continuous variables and Chi-square test for categorical variables. Independent *t*-test was used to measure the difference in difference of the intervention and control groups at baseline and end line for the clinical outcome indicators including pain crisis, hospitalization, blood transfusion, and average hemoglobin. Similar to the baseline, *t*-test was used for continuous variables and Chi-square test for the categorical variables to measure the end line characteristics for other variables. SPSS version 20.0 (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) was used for the data analysis.

Ethical issues

This study received ethical clearance from the SEWA Rural Institutional Ethics Committee before the study. Written, informed consent was attained from the participants and parents of the participants in the case of minors.

To secure the privacy of the respondents, we masked dataset with a unique ID. We removed all personally identifiable information from the dataset. The dataset was only accessible to the investigators. The hard copies are saved under the security of a locker and only investigators have access to keys.

Results

We received a line listing of 716 SCD patients from the government registry. After exclusion, 293 and 273 patients were allocated, respectively, in the intervention and control groups. A survey team visited them at their respective homes for baseline data collection. A total of 101 patients in the control group and 84 patients in the intervention group were recruited in the study [Figure 2]. All patients were from the Scheduled Tribal population, with 103 (54.8%) females. Overall, 142 (76.6%) patients were below the poverty line, and the literacy rate was 92% [Table 2]. Among the intervention group, 29 (34.5%) patients were lost to follow-up. Total 14 (13.7%) members of the control group were registered in the sickle cell registry during intervention period.

Knowledge of SCD was comparable in both arms at baseline. There was a significant improvement in the intervention group at end line as compared to the control group [Table 3]. Regarding QoL, the intervention group as compared to the control group had improvement in "health compared to last year," "improvement in health," "ability to do vigorous activities," and "satisfaction at work and school" and decrease in "limit to work because of physical health since last 1 month," "painful crisis since last month," "feeling of downhearted and blue most of the time due to SCD," and "lost school or work due to disease" [Table 4].

The coverage of proven interventions at baseline and endline were presented in Tables 5 and 6. At baseline, none of the

Table 2: Sociodemographic characteristics study of hospital-based comprehensive sickle cell disease program in tribal area of Gujarat, India, 2016–18

Characteristic	Categories	Intervention (n=84), n (%)	Control (n=101), n (%)	P***
Gender	Male	37 (44.0)	45 (44.6)	0.945
	Female	47 (56.0)	56 (55.4)	
Caste	ST	84 (100.0)	101 (100.0)	
Age (years)	0–5	0	0	0.712
	6–20	60 (71.4)	67 (66.3)	
	21–40	24 (28.6)	34 (33.7)	
Education	Illiterate	8 (9.5)	6 (5.9)	0.829
	Primary (1–8 standard)	52 (61.9)	63 (57.9)	
	Secondary or higher (>8 standard)	24 (28.6)	32 (36.2)	
Marital status	Unmarried	65 (77.4)	72 (71.3)	0.441
	Married	17 (20.2)	27 (26.7)	
	Widow	1 (1.2)	1 (1.0)	
	Divorcee	1 (1.2)	0	
	Separated	-	1 (1.0)	
Economic condition	Have BPL card	67 (79.8)	75 (74.3)	0.377

***Chi-square test was used to determine the significance of difference among the groups. Boldface indicates statistical significance (P<0.05). BPL card: Below poverty line card, ST: Scheduled Tribe

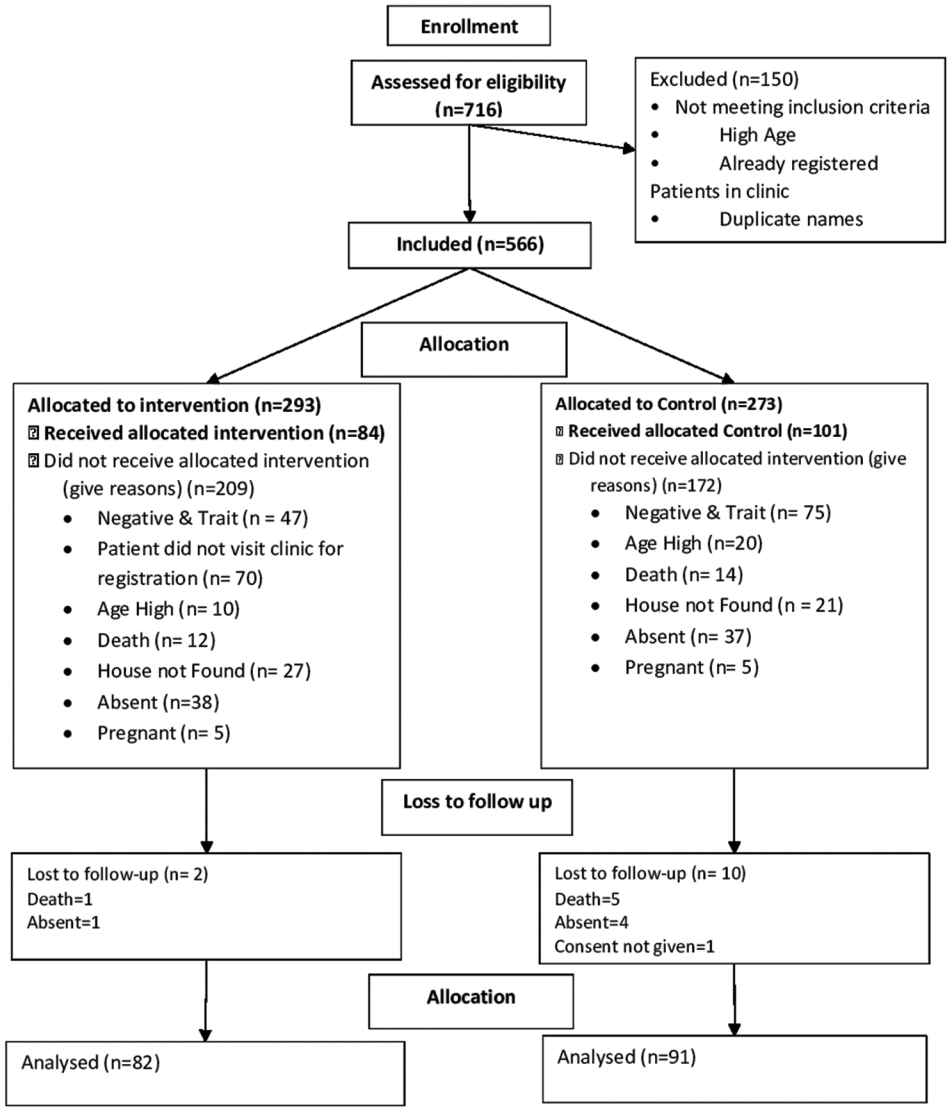

Figure 2: Flow diagram of the study

severe SCD patients were taking HU. At baseline, the coverage of proven interventions including pneumococcal vaccination (Odds ratio OR 1.0 [95% CI 0.99–1.04], $P = 0.454$), and CHQ (OR: 2.4 [95% CI 0.2–27.4], $P = 0.591$), were similar in both groups. At endline, there have been significant improvement in the intervention group in compared to control groups in coverage of proven interventions including HU medicine for severe SCD patients (OR 7.1 [CI 1.8–28.6], $P = 0.002$), pneumovax vaccination (OR 21.3 [95% CI 9.7–46.8]), $P = 0.000$, CHQ (OR 4.9 [95% CI 2.4–10.2], $P = 0.000$), and folic acid (OR 4.1 [95% CI 2.2–7.8]), $P = 0.000$).

We measured change in clinical outcomes from baseline to endline in both groups. The change in intervention group compared to control group was not significant for the clinical outcomes including pain crisis (mean difference [MD]: −0.18 [−1.17–0.812]), $P = 0.719$, hospitalization rate (MD: −0.08 [−0.375–0.210]), $P = 0.576$, and blood transfusion (MD: −0.60 [−0.532–0.412]), $P = 0.803$, and minor improvement in hemoglobin level (MD: −0.25 [−0.300–0.811]), $P = 0.$ 0.365. The result of phone call follow-ups for clinical outcome indicators is presented in Appendix Table 1.

Discussion

In this study, we describe the effectiveness of a hospital-based comprehensive SCD program for SCD patients. Coverage of proven interventions improved including vaccination and HU adherence among severe SCD patients, as well as knowledge about SCD among patients. The improvement in outcome indicators, which include pain crises, hospitalizations, blood transfusions, and hemoglobin level, were marginal at end line in the intervention group as compared to the control group. There was a marginal improvement in the QoL in the intervention group as compared to the control group.

Various mHealth intervention models have been effective for chronic disease and SCD management in high-income

Table 3: Effectiveness of hospital-based comprehensive sickle cell disease program on sickle cell disease-related knowledge in tribal area of Gujarat, India, 2016–2018 (*n*=173)

Characteristic	Baseline				End line			
	Intervention (*n*=84), *n* (%)	Control (*n*=101), *n* (%)	OR (95% CI)	*P***	Intervention (*n*=82), *n* (%)	Control (*n*=91), *n* (%)	OR (95% CI)	*P***
Knowing their SCD status	36 (42.9)	45 (44.6)	0.9 (0.5–1.7)	0.817	81 (98.8)	76 (83.5)	**16.0 (2.1–124.0)**	**0.001**
Knowing at least one symptom of the SCD	25 (29.8)	37 (36.6)	0.7 (0.4–1.4)	0.324	73 (89)	68 (74.7)	**2.7 (1.2–6.4)**	**0.016**
Knowing at least one precautionary step to prevent SCD complication	18 (21.4)	22 (21.8)	0.98 (0.5–1.98)	0.954	59 (72)	46 (50.5)	**2.5 (1.3–4.7)**	**0.004**
Knowing that SCD is hereditary disease	14 (16.7)	5 (5.0)	**3.8 (1.3–11.2)**	**0.009**	24 (29.3)	6 (6.6)	**5.8 (2.3–15.2)**	**0.000**

**Chi-square test was used to determine to significance of difference among the groups, ***Boldface indicates statistical significance ($P<0.05$). OR: Odds ratio, CI: Confidence interval, SCD: Sickle cell disease

Table 4: Effectiveness of hospital-based comprehensive sickle cell disease program on quality of life in tribal area, Gujarat, India, 2016–2018

Variable characteristics	Indicator	Baseline			End line			Absolute difference in difference for change
		Intervention (*n*=84), *n* (%)	Control (*n*=101)	*P***	Intervention (*n*=82), *n* (%)	Control (*n*=91), *n* (%)	*P***	
How is your health since the last 1 year?	Good	79 (94)	95 (94.1)	0.671	74 (90.2)	75 (82.4)	0.102	7.9
Compare health with previous year	Better	25 (29.8)	27 (26.7)	0.384	59 (72.0)	46 (50.5)	**0.003**	18.4
Able to do vigorous activities	Yes	64 (76.2)	77 (76.2)	0.565	64 (78.0)	64 (70.3)	0.163	7.7
Able to do moderate activities	Yes	82 (97.6)	101 (100)	0.119	78 (95.1)	89 (97.8)	0.293	−0.3
Limit in work because of physical health (4 weeks)	Yes	13 (15.5)	7 (6.9)	0.052	15 (18.3)	19 (20.9)	0.408	−11.2
Missed any social function because of physical health	Yes	5 (6.1)	6 (5.9)	0.617	15 (18.3)	19 (20.9)	0.408	−2.8
Pain in the last month	Yes	14 (16.7)	16 (15.8)	0.518	16 (19.5)	24 (26.4)	0.187	−7.8
Patient felt downhearted and blue most of the time	Yes	6 (7.1)	3 (3.0)	0.166	6 (7.3)	14 (15.4)	0.077	−12.2
Patient felt tired most of the time	Yes	7 (8.3)	2 (2)	0.048	6 (7.3)	14 (15.4)	0.077	−14.4
Patient satisfied at work/school	Yes	79 (94.0)	100 (99)	0.069	79 (96.3)	87 (95.6)	0.558	5.7
Lost work or left schooling due to disease?	Yes	12 (14.3)	7 (6.9)	0.081	22 (26.8)	33 (36.3)	0.121	−16.9

**Chi-square test was used to determine to significance of difference among the groups, significant if $P<0.05$, we used Fisher's exact test, whenever the assumptions of Chi-square did not satisfy, ***Absolute difference in difference for change: Proportion in (intervention end line + control baseline – [intervention baseline + control end line]), ****Bold face indicates statistical significance ($P<0.05$). SCD: Sickle cell disease

Table 5: Coverage of proven interventions at hospital-based comprehensive sickle cell disease program in tribal area of Gujarat, India, 2016–2018

Characteristics	Baseline		OR (95% CI)	*P*	End line		OR (95% CI)	*P*	Absolute difference in difference for change***
	Intervention (84), *n* (%)	Control (101), *n* (%)			Intervention (82), *n* (%)	Control (91), *n* (%)			
Pneumococcal 23V vaccine	1 (1.2)	0	1.0 (0.99–1.04)	0.454	64 (78)	13 (14.3)	21.3 (9.7–46.8)	**0.000**	62.5
Folic acid taken yesterday	23 (27.4)	13 (13)	2.6 (1.2–5.4)	**0.016**	51 (62.2)	26 (28.6)	4.1 (2.2–7.8)	**0.000**	19.2
CHQ received last week	2 (2.4)	1 (1.0)	2.4 (0.2–27.4)	0.591	37 (45)	13 (14.3)	4.9 (2.4–10.2)	**0.000**	29.3
HU received last week**	0	0	-	-	10 (32)	3 (6.2)	7.1 (1.8–28.6)	**0.002**	25.8

***n*-baseline: Intervention - 14, control - 24, end line: Intervention - 31, control - 48, ***Absolute difference in difference for change: Proportion in (intervention end line+control baseline – [intervention baseline + control end line]), ****Boldface indicates statistical significance ($P<0.05$). SCD: Sickle cell disease, OR: Odds ratio, CI: Confidence interval, HU: Hydroxyurea

Table 6: Effectiveness of hospital-based comprehensive sickle cell disease program on clinical outcomes at in tribal area, Gujarat, India, 2016–2018

Characteristics	Baseline						End line						DID (IE-IB) – (CE-CB)* (*n*=173)	
	Intervention (84)		Control (101)		Mean difference (95% CI)	*P*	Intervention (*n*=82)		Control (*n*=91)		Mean difference (95% CI)	*P*	Mean difference (95% CI)	*P*
	Mean	SD	Mean	SD			Mean	SD	Mean	SD				
Pain crisis	1.2	1.5	1.7	2.4	−0.51 (−1.09–0.56)	0.077	2.2	2.9	2.9	3.4	−0.7 (−1.63–0.29)	0.168	−0.18 (−1.17–0.812)	0.719
Hospitalization	0.26	0.96	0.14	0.38	0.12 (−0.10–0.34)	0.269	0.32	0.68	0.29	0.67	0.03 (−0.17–0.24)	0.761	−0.08 (−0.375–0.210)	0.576
Blood transfusion	0.18	1.5	0.09	0.4	0.09 (−0.22–0.40)	0.573	0.24	1.2	0.21	0.98	0.035 (−0.29–0.36)	0.832	−0.60 (−0.532–0.412)	0.803
Average Hb	8.7	1.5	9.0	2.0	−0.31 (−0.83–0.20)	0.229	8.94	1.8	8.99	1.9	0.05 (−0.61–0.51)	0.860	0.25 (−0.300–0.811)	0.365

OR: Odds ratio, CI: Confidence interval, SD: Standard deviation, SCD: Sickle cell disease, *[intervention end line - intervention baseline] – [control end line- control baseline]

countries.[24,25] However, the effectiveness of mHealth strategies has not been well studied in India and other low- and middle-income countries. Similar to our study, a study performed in Chicago found that hospital-based quality improvement led to improvements in the prescription of HU, vaccination coverage, and laboratory monitoring.[26] Press *et al*. mentioned that a dedicated primary care physician-led sickle cell outpatient clinic leads to a decrease in annual hospitalization rate.[27] In a previous study, we found that hospital admission during registration, patients with a history of vaso-occlusive crisis, and being married were associated with loss to follow-up.[28] In this study, follow-up by telephone was conducted to improve follow-up rates for patients who did not visit clinic regularly. The telephone call follow ups by non medical personals improves adherence to care among SCD patients.[29]

The improvement in coverage of intervention might be due to the availability of comprehensive free care under one roof. The adherence to care among the intervention group might be improved by follow-up calls by the counselor backed by an IT-based application. Data were collected in both the groups through telephone calls every 4 months; this could have introduced Hawthorne effect and influenced results in both the groups.[30] In addition, HU was administered at fixed dose (10 mg/kg/day) and not at maximum tolerable dose; this might have led to a limited, diluted effect on the clinical outcomes in the intervention group.

A strength of this study is that it provides evidence on the effectiveness of a comprehensive hospital-based SCD care model supported with IT system on various components including coverage of proven intervention, knowledge of the patients, clinical outcomes, and QoL. To our knowledge, this is the first study in the Indian context to use mHealth as a case management aid for health workers managing SCD.

Conclusion

This study demonstrates that a hospital-based comprehensive care model supported by a web application platform has great potential to improve coverage of proven interventions for SCD, especially in hard-to-reach areas with a lack of resources and where the burden of SCD is high. Further randomized trials are needed to measure the effectiveness of the hospital-based comprehensive care on clinical outcomes.

Acknowledgments

We are thankful to all the participants and respondents, to Dr. Ankit Anand for his contribution toward finding a sample size for the study, to Dr. Kala Mehta for her initial inputs during the development of this study, to the Kasturba Hospital (SEWA Rural) staff for providing health care to SCD patients, to Mr. Jitendra Joshi for his involvement in the management of the IT system, to Dr. Somen Saha for his guidance during analysis, to Dr. Somali Benerjee and Dr. Palav Babaria for their support in study design, and to Shital Shah for proofreading of the manuscript.

Financial support and sponsorship

Anupam Rasayan India Ltd. funded this study.

Conflicts of interest

There are no conflicts of interest.

References

1. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. Lancet 2010;376:2018-31.
2. Wang Y, Liu G, Caggana M, Kennedy J, Zimmerman R, Oyeku SO, *et al.* Mortality of New York children with sickle cell disease identified through newborn screening. Genet Med 2015;17:452-9.
3. Desai G, Anand A, Shah P, Shah S, Dave K, Bhatt H, *et al.* Sickle cell disease and pregnancy outcomes: A study of the community-based hospital in a tribal block of Gujarat, India. J Health Popul Nutr 2017;36:3.
4. 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;36:316-22.
5. Colah RB, Mukherjee MB, Martin S, Ghosh K. Sickle cell disease in tribal populations in India. Indian J Med Res 2015;141:509-15.
6. Patel J, Patel B, Gamit N, Serjeant GR. Screening for the sickle cell gene in Gujarat, India: A village-based model. J Community Genet 2013;4:43-7.
7. Saxena D, Yasobant S, Golechha M. Situational analysis of sickle cell disease in Gujarat, India. Indian J Community Med 2017;42:218-21.
8. Colah R, Mukherjee M, Ghosh K. Sickle cell disease in India. Curr Opin Hematol 2014;21:215-23.
9. Lee A, Thomas P, Cupidore L, Serjeant B, Serjeant G. Improved survival in homozygous sickle cell disease: Lessons from a cohort study. BMJ 1995;311:1600-2.
10. Gaston MH, Verter JI, Woods G, Pegelow C, Kelleher J, Presbury G, *et al.* Prophylaxis with oral penicillin in children with sickle cell anemia. A randomized trial. N Engl J Med 1986;314:1593-9.
11. Vichinsky E, Hurst D, Earles A, Kleman K, Lubin B. Newborn screening for sickle cell disease: Effect on mortality. Pediatrics 1988;81:749-55.
12. Yawn BP, John-Sowah J. Management of sickle cell disease: Recommendations from the 2014 expert panel report. Am Fam Physician 2015;92:1069-76.
13. National Health Mission. Sickle Cell Anemia Control Program Common Symptoms of Sickle Cell Anemia Sickle Cell Anemia in India; 2015. Available from: https://nhm.gujarat.gov.in/sickle-cell.htm. [Last accessed on 2020 Oct 24].
14. 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.
15. Yawn BP, Buchanan GR, Afenyi-Annan AN, Ballas SK, Hassell KL, James AH, *et al*. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members [published correction appears in JAMA 2014;312:1932] [published correction appears in JAMA 2015;313:729]. JAMA 2014;312:1033-48. doi:10.1001/jama.2014.10517.
16. Platt OS, Thorington BD, Brambilla DJ, Milner DJ, Rosse PF, Vichinsky WF, *et al*. Pain in sickle cell disease. Rates and risk factors. N Engl J Med 1991;325:11-6. doi:10.1056/ NEJM199107043250103.
17. Signorelli AA, Ribeiro SB, Moraes-Souza H, de Oliveira LF, Ribeiro JB, da Silva SH, *et al.* Pain measurement as part of primary healthcare of adult patients with sickle cell disease. Rev Bras Hematol Hemoter 2013;35:272-7.
18. Darbari DS, Sheehan VA, Ballas SK. The vaso-occlusive pain crisis in sickle cell disease: Definition, pathophysiology, and management. Eur J Haematol 2020;105:237-46.
19. Léger D, Scheuermaier K, Philip P, Paillard M, Guilleminault C. SF-36: Evaluation of quality of life in severe and mild insomniacs compared with good sleepers. Psychosom Med 2001;63:49-55.
20. World Health Organization. WHO | WHOQOL: Measuring Quality of Life. Health statistics and information systems (WHO). Geneva 27,

Switzerland, World Health Organization; 2014. p. 1.
21. Thabane L. Sample Size Determination in Clinical Trials HRM-733 Class Notes; 2004. Available from: http://www.lehanathabane.com. [Last accessed on 2021 Jun 19].
22. Columbia University Mailman School of Public Health [Internet]. Difference-in-Difference Estimation. 2016. Available from: https://www.publichealth.columbia.edu/research/population-health-methods/difference-difference-estimation [Last cited on 2023 Jul 08].
23. Rubin DB. Randomization Analysis of Experimental Data: The Fisher Randomization Test Comment. Journal of the American Statistical Association 1980;75:591-3.
24. World Health Organization. MHealth New Horizons for Health through Mobile Technologies. Vol. 3. Geneva 27, Switzerland, World Health Organization; 2011.
25. Badawy SM, Cronin RM, Hankins J, Crosby L, DeBaun M, Thompson AA, *et al.* Patient-centered eHealth interventions for children, adolescents, and adults with sickle cell disease: Systematic review. J Med Internet Res 2018;20:e10940.
26. Artz N, Whelan C, Feehan S. Caring for the adult with sickle cell disease: Results of a multidisciplinary pilot program. J Natl Med Assoc 2010;102:1009-16.
27. Press A, Lucito R, Friedman I, Ginzburg S. A clinic to improve care of patients with sickle cell disease and the role of medical students in quality improvement. Blood 2015;126:5586.
28. Dave K, Chinnakali P, Thekkur P, Desai S, Vora C, Desai G. Attrition from care and clinical outcomes in a cohort of sickle cell disease patients in a tribal area of Western India. Trop Med Infect Dis 2019;4:125.
29. Patik M, Phillips L, Kladny B, Captain A, Gettig E, Krishnamurti L. Structured telephone-based outreach using nonmedical personnel can improve adherence to comprehensive care in families of children with sickle cell disease. Am J Hematol 2006;81:462-4.
30. McCambridge J, Witton J, Elbourne DR. Systematic review of the Hawthorne effect: New concepts are needed to study research participation effects. J Clin Epidemiol 2014;67:267-77.

Appendix

Appendix Table 1: Clinical outcomes as per telephonic-calls among registered SCD* patients in tribal-area of Gujarat-India at year 2016-18

Characteristics	Baseline				1 Year of intervention				2 Years of intervention			
	Intervention (*n*-84)		Control (*n*-101)		Intervention (*n*-79)		Control (*n*-88)		Intervention (*n*-79)		Control (*n*-88)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Pain crisis	1.2	1.5	1.7	2.4	0.4	0.9	1.1	1.7	1.2	1.97	1.6	2.0
Hospitalization	0.26	0.96	0.14	0.38	0.1	0.40	0.1	0.4	0.4	1.0	0.18	0.5
Blood transfusion	0.18	1.5	0.09	0.4	0.0	0.0	0.0	0.0	0.1	0.5	0.05	0.21

*SCD- sickle cell disease