Adherence patterns among patients receiving healthcare services in the Muhimbili Sickle Cell Cohort, Tanzania

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Abstract

Background: Monitoring of patient's clinical attendance is one of the crucial means that is used to improve adherence to care and treatment among the Sickle Cell Disease (SCD) patients. Adherence to care has been shown to improve health outcomes in SCD patients. However, these benefits cannot be achieved when patients are lost to follow-up to care. Method : We analyzed data on loss to follow up to determine the patterns among sickle cell patients registered at Muhimbili Sickle Cell Cohort (MSC), in Dar es Salaam, Tanzania. Data was aggregated and analysed using R software and Microsoft Excel Spreadsheet. Survival analysis techniques, both non-parametric methods (Kaplan-Meier estimator and Log-rank test) and semi-parametric method (Cox's proportional hazard model), were used. A p-value of 0.05 was considered significant to make a strong inference of the analysis. Results: 5476 SCD patients were registered at MSC from 2004 to 2016, 3350 (58.13%) were actively participating in clinics while, 2126 (41.87%) were inactive, out of which 35.19% were lost to follow-up. From the survival analysis results, patients who were between 5 to 17 years were more likely to be lost to follow-up than the rest with a hazard ratio of 2.65 times more than those who were above 18 years. Patients with mean cell volume above 77.73 fL and white blood cell above 15.73(10ˆ3/uL) were more likely to be loss to follow-up than those below average. Conclusion: Loss to follow-up is evident in a cohort of patients in long term comprehensive care follow-up. It is, therefore, necessary to design interventions that minimize its impacts. Suggested solutions might include training of the health care workers, more emphasis on newborn screening and advocacy to patients regarding the effect of loss to follow-up.

Background

Sickle cell disease (SCD) is an inherited disease caused by a single-gene mutation affecting the β-globin gene (HBB) on chromosome 11. It results in an abnormality of red blood cells (RBC), which affects their shape and function, and subsequently influencing nearly all organ systems of the body(1). SCD is one of the most prevalent inherited blood disorders with the highest-burden in Africa, where up to 75% of the 300,000 global births of SCD per year occur(2). It is estimated that 50–80% of infants born with SCD in Africa die before the age of 5 years(3). SCD impacts both patients and societies in general, by a way of reduction in quality of life, high morbidity and mortality, which led to financial burdens to individuals, families and health care(1)(4).

Studies have shown that sickle cell clinics have substantially improved the health of sickle cell patients through the provision of comprehensive care, that involves supplying patients with folic acid, treated nets, anti-malarial chemoprophylaxis and other services such as health education and counseling(5). Children under the age of six are provided daily with oral penicillin and pneumococcal conjugate vaccine (PCV), which prevents severe pneumonia episodes, which was reported as a leading cause of morbidity and mortality to children of that age (6). Information collected during the SCD follow-up clinics includes demographic, clinical, physiological and laboratory data. This recorded information is very crucial in assessing and ultimately counseling patients, choosing the appropriate medical treatment, evaluating the accuracy of clinical research, and definition of disease severity(1)(7). Adherence to comprehensive care has been shown to improve health outcomes in SCD patients and decrease health care resource utilization(8). However, these benefits cannot be achieved when patients are lost to follow-up to comprehensive care.

Loss to follow-up events remains to be one of the significant challenges facing most clinical cohort studies, whereby patients tend not to fully participate in the clinics(9). Most of the Sickle cell patients tend to attend clinic when they face complications as a result of having the disease. Several factors contribute to the loss of follow up among patients such as financial problems, being in good health and long distance from the clinic to the patient home(9)(10)(11). When analyzing cohort data with many losses to follow-up (LTFU) events, bias is likely to be encountered since some crucial information may be left out because these events are usually not random.

Consequently, the effectiveness of treatments will not be correctly assessed (7)(12). When SCD patients, do not attend clinics as scheduled, their treatment will be interrupted and hence could lead to more health complications. Therefore, assessing the loss to follow-up patterns is essential to improve the overall performance of cohort treatment and the patient's health. We now describe the loss to follow-up patterns among sickle cell patients registered at Muhimbili Sickle cell Cohort (MSC)

Method

Study Design and Site

This study is based on data of SCD patients registered at MSC. The cohort was established in the year 2004 by the Muhimbili National Hospital (MNH) in collaboration with Muhimbili University of Health and Allied Sciences (MUHAS), the oldest and largest biomedical university in Tanzania. The MSC was established to provide a clinical spectrum of sickle cell disease, identify causes of morbidity and mortality and to develop strategies for appropriate interventions.

Study population

Muhimbili National Hospital has an existing health service with dedicated SCD clinics for children and adults. In 2004, this framework was used to develop a platform for the integrated approach called Muhimbili Sickle Cell Cohort (MSC). Between March 2004 and March 2016, a total of 8484 individuals were seen and given unique demographic identity numbers. Screening for SCD was done by the sickling test, which uses sodium metabisulphite. A total of 5476 (64%) individuals were confirmed HbSS, 2121 (25%) with sickle cell trait (HbAS) and 897 (11%) had normal hemoglobin pattern (HbAA). Apart from a few patients with S/β-thalassemia, more than 99% of patients have homozygous (SS) SCD. Individuals who were confirmed to have SCD were enrolled in the MSC. The registered patients were assigned a unique SCD identification number.

Cohort Description

From the inception of MSC (2004) up to 2016 around 5476 (figure 1), sickle cell patients were enrolled at Muhimbili sickle cell cohort (MSC). Out of the total registered patients, 2797 (51.08%) were males while females were 2679 (48.92%) as shown in Table 1. The minimum age at registration was less than 1 year 402(7.34%) while the majority of registered patients were children between 5 to 17 years old (45.38%). Regarding the place of birth, most of the enrolled patients were born in the Coastal regions (72.92) which include Dar es Salaam. Out of 366 reported deaths (figure 1), children under five years were 36.34%while those between 5-17 years were 45.35%.

Table 1: Demographics Characteristics of SCD patients who were enrolled at Muhimbili Sickle Cohort

	Total
All SCD	5476
Age groups	
0-4	2294(41.89%)
5-17	2485 (45.38%)
18+	680 (12.42%)
Gender	
Female	2679 (48.92%)
Male	2797 (51.08%)
Place of Birth	
Coastal Regions	3993(72.92%)
Others	1476 (26.95%)
Missing	7 (0.13%)

Fig.2 shows the annual trend of enrollment and loss to follow-up patterns from 2004 to 2016. The highest number of registration was done at the beginning of the study (2004) while loss to follow up events appears to be increasing as time goes with a maximum peak in 2015. During this year, SCD patients were referred to government hospitals to attend SCD clinics away from the MSC at MNH. In our analysis, we considered visits up to 2014 since people who are referred to other hospitals cannot be categorized as loss to follow-up. The number shown at the top of the blue bars present the total number of lost to follow-up events at each respective year. The line on the top of the bar plot represents a cumulative enrollment of SCD patients from 2004 to 2016.

Sampling

A total of 5476 patients were confirmed of their HbSS status and were enrolled at MSC between 2004 to 2016. Three sets of data were collected; one on visit dates and demographic information, clinical results (patient's routine checks) and test results (hematological parameters). The three datasets were merged based on the unique demographic id, visit id and visit date.

It should be noted that clinical and hematological information was not taken at every clinic visit, some visits only recorded basic information. Hence during data merge, we found missing values that were taken care with missing values techniques. Patients were divided into two groups; active (not missing clinics more than nine-month between consecutive clinics) and inactive (miss clinics more than months between consecutive clinics and did not attend clinic for the last 9 months with reference to 30/12/2016). As shown in Fig.1, a total of 3183 (58.13%) were actively participating in the clinic while 2293 were inactive due to reasons like they are deceased or dropping out of the study. From the inactive group, 366 (6.68%) were identified as deceased and 1925 (35.19%) classified as LTFU.

Study Outcome and exposure

The primary outcome was loss to follow-up (LTFU) event, which was defined as no clinic attendance for at least nine months with reference to the patient's previous clinic attendance date. This was decided based on a practice of 3-6 months between clinic appointments.

Data management and analysis

Data from the MSC collected between the years 2004-2016 was used in this analysis. The investigation was done using R Studio 1.2.5033 and Microsoft Excel spreadsheets. Survival analysis techniques, both non-parametric methods (Kaplan-Meier estimator and Log-rank test) and semi-parametric method (Cox's proportional hazard model) were used. A P-value cutoff of 0.05 was used to ascertain the statistical significance of the obtained results.

Analysis assumptions

The following analysis assumptions were used in our study. SCD patient who did not attend clinic for more than nine months with reference to the previous clinic attendance date was classified as LTFU. Time in the study was taken as a difference between the first clinic attendance date and the last day. For the analysis we have used an event record that is close to the last attendance date for the patient while age was calculated twice at registration and at the time of LTFU event which was used for the analysis. Furthermore, patients who were reported dead and those who were present in the last window of nine-month (a reference to 30/12/2016) were censored. All survival times were assumed independent and censoring occurred at the right censor.

Results

Table 2 shows different clinical and laboratory features between sickle cell patients who were lost to follow-up and those who were not. The test statistics column shows t-test statistics comparison for different attributes between SCD patients who were lost to follow-up and those who were not. Based on the p-values the statistical difference between the two groups was notable with age, mean cell volume (mcv) and mean cell hb concentration (mchc). The level of mcv was slightly higher for those patients who were lost to follow-up compared to those who were not.

Table 2: Laboratory and clinical features for patients who are lost to follow-up versus those who are not.

Fig.3 on the left shows the overall survival probability of SCD patients over time with a 95% confidence interval using the Kaplan-Meir method. At the beginning of the study, the survival probability is 1 since no LTFU events have occurred, the curve is horizontal up to around 300 days which is more than 9 months. The median survival time, a point at which half of the patients are LTFU happens to be 2848 days (7.8 years) with a 95% confidence interval of [2716-3004] days. By 2013, which is ten years from the beginning of the MSC, the survival probability is around 0.2113. The curve on the right in Fig.3 shows cumulative loss to follow-up events at different time points among sickle cell patients. This graph shows the cumulative number of people who were lost at a specific point in time.

In addition to the overall survival trend for all SCD patients, we compared the survival probabilities for different groups in the study. The LogRank test and Cox's hazard analysis with a significant level of 5% were used to achieve this purpose. Fig.4 shows different survival curves for different groups in our data. The first graph on the left shows a comparison between three age groups categories in our data. The first age group (agegrp1)

	NOT LTFU			LTFU			Test Statistics
	Mean	Median	IQR	Mean	Median	IQR	(P-value)
Age	14.23	13	07.00-19.00	12.36	11	07.00-15.00	t = 5.696 (<0.001)
White blood cell (10^3/uL)	14.34	13.11	10.69-16.60	14.57	13.65	10.90-17.19	t=-0.9953(0.3197)
Neutrophils (%)	46.8	46.5	38.80-54.52	45.89	45.2	38.10-53.25	t=1.9524(0.0509)
Hemoglobin (g/dL)	7.46	7.4	6.60-8.30	7.45	7.4	6.70-08.20	t=0.0620(0.9505)
Red Blood Cells ((10^6/uL)	2.93	2.85	2.42-3.33	2.93	2.83	2.44-3.28	t=0.1212(0.9036)
Mean Cell Volume (fL)	78.43	78.58	72.00-85.20	77.48	77.4	71.50-83.80	t=2.3742(0.0177)
Mean Cell Hb Concentration (g/dL)	33.22	33.3	31.60-34.90	33.57	33.8	32.27-35.10	t=-4.0359(<0.001)
Red Cell Distribution Width (%)	22.41	22	19.70-24.40	22.48	22.3	19.80-24.70	t=-0.2216(0.8247)
Platelets (10^3/uL)	422.36	417	304-522	422.8	409.5	312-522	t=-0.0655(0.9478)
Haematocrit (%)	22.47	22.2	19.70-22.20	22.21	21.8	19.60-24.50	t = 1.5341(0.1251)

represents sickle cell patients who are 18 and above, agegrp2 those who are 5 to 17 and agegrp3 children who are between 0 to 4. Based on the graph patients who are 18+ are least likely to be LTFU, followed by those who are between 5 to 17 and children under 5 with the highest proportion of LTFU. This difference in survival times on age groups was significant with a p-value less than 0.05. Table 3 shows the hazard ratios from the Cox proportional hazard model, with the age group patients who are 18+ used as a reference group. From obtained results, the hazard of patients aged 5 to 17 years is 2.61 times higher than those above 18 while for children under 5 is 14.29 times higher than those above 18+.

In the cox model, painful and fever attributes were removed due to lack of independence with the age group (agegrp) and well today attributes. Through the chi-square test, age group and painful attributes were found to depend on one another with a p-value of 8.889e-07 and the same observation was with fever and well today(p-value= 5.96e-07). Thus being the case their survival curves are being displayed but not their corresponding hazard ratio except for well today. As depicted in Fig.4 patients who experience painful episodes were least likely to be lost to follow-up compared to those with no painful episodes. A different pattern is observed with the fever attribute whereby patients with fever were more likely to be loss to follow-up than those with no fever. For the well today attribute the hazard ratio of those who are well was 13.31% higher than those who are not well. Looking at the white blood cell count (wbc), a hazard ratio of patients with wbc above average value (14.34) is 1.58% higher than those below average. This means those with wbc above average count a more likely to be loss to follow-up than those below the average value. Patients with hematocrit count above average value (22.69) have a hazard ratio of 2.38% higher than those with a value below average. This means those hematocrit values above average are more likely to be loss to followup than those below average.

Table 3. Final results of the Cox proportional hazard model with significant attributes

Attribute	Estimate	hazard ratio	Pr(>|z|)	lower 0.95	Upper 0.95
White blood cells (10^3/uL)	0.0157	1.0158	0.0074	1.0042	1.0276
Hematocrit (%)	0.0235	1.0238	0.0039	1.0076	1.0404
Well today (Yes)	0.1249	1.1331	0.0495	1.0003	1.2837
Age group (5-17)	0.9624	2.6181	< 2E-16	2.2324	3.0705
Age group (<5)	2.6602	14.2995	< 2E-16	11.0071	18.5768
mch:time_group(0-2050 days)	-0.1286	0.8792	2.57E-08	0.8403	0.92
mch:time_group(>2050)	0.0073	1.0073	0.8265	0.9432	1.0759
mcv:time_group(0-2050 days)	0.0419	1.0428	4.02E-07	1.026	1.0598
mcv:time_group(>2050)	-0.0005	0.9994	0.9629	0.9745	1.0249

During model fitting mean corpuscular hemoglobin (mch) and mean cell volume (mcv) were found to be highly significant but violating proportionality assumption. To rectify this, stratification of their variable was performed by splitting the follow-up period. Table 5 shows results of proportionality assumptions after stratification whereby all attributes are seen to satisfy this assumption. We did consider two follow-up intervals, one from 0-2050 days and 2050 to the end of the study. Based on the obtained results in Table 4 the effect of mcv and mch to loss to follow-up pattern is limited to the first time period (0 to 2050 days). This means between 0 to 2050 of attending clinics patients with mcv value above average (77.73 fL) have a hazard ratio of 4.28% higher than those below average and hence patients with mcv above are more likely to be loss to follow-up than those below the average value. With the mch, patients with mch value higher than average value have a hazard ratio of 12% less than those below the average value. This means they are less to be lost to follow up than those below the average value.

Discussion

This is the report describing factors associated with loss to follow-up patterns in a large cohort of sickle cell patients receiving care at Muhimbili hospital in Tanzania. We analyzed loss to follow-up patterns among sickle cell patients registered at Muhimbili Sickle cell Cohort (MSC) from 2004-2014. The rate of loss to follow-up was around 35.19% which according to one author presents no important bias from 5% to 60% (13). The cumulative incidences of loss to follow-up increase as the duration of MSC increase shows the importance of measures such as sending reminders and counseling on adherence to clinics. Children have high rates of loss to follow-up due to several factors including complications related to the disease as cited by one author (10). This signifies the need for early interventions such as tracing them to prevent the burden of early childhood mortality rate(10).

Through the use of survival analysis techniques, interesting loss to follow-up patterns among sickle cell patients were discovered. For example, patients who are between 5 and 17 were more likely to be loss to follow-up than those who are 18+. Issues unique to adolescence (5-17 years) include schooling demands like migrating to boarding schools and the general transition to adulthood entailing moving to other places looking for a job. A similar pattern is seen with patients under five who were found with higher hazards of loss to follow-up than those above 18+. Several factors can account for this such as death at a young age as a result of disease complications or migrating to new places. From the 366 reported deaths, 36.34% were between 0-4

years while 45.35% were 5-17 years and 18.31% were for those 18 and above. A different pattern was observed with fever whereby people with fever were more likely to be loss to follow-up than those with no fever. The assumption for this was that people are probably going to nearby health facilities such as pharmacies to buy medicine to low down fever rather than waiting for clinic day.

Patients who were not feeling well were least likely to be loss to follow-up than those who are well which is expected due to the need for contact with the healthcare system, as was the case for those with pain who were less likely to be lost to follow-up than those with no painful episodes. These clinical parameters are congruent with some of the observed hematological parameters. Patients with hematocrit (percentage of red blood cell) and mean cell volume (mcv) above the average value are more likely to be loss to follow-up than those with below average value. These correspond to a lesser likelihood of anemia complications and consequently, feeling well. But a different pattern was observed with mch whereby those with a value above average were least likely to be loss to follow-up than those below average. One assumption could be made for this pattern as they are sick to a point they miss their clinical appointment. According to one author increase in white blood cell count is associated with an increase in the number of complications in sickle cell and in our findings we discovered that those with a value above average were more likely to be lost follow-up (14). The following assumption can be made that they are sick to a point they missed their appointments or the got sick before the appointment day and they were treated in other health facilities.

Hence we can conclude that loss to follow-up in cohort studies is still a problem and necessary interventions are needed to be put into a place. When LTFU rates become high, the health of the patient is compromised together with the study validity such as assessment of the medical treatment and study results. For the case of our study, the LTFU events were randomly and as demonstrated by one author no bias when LTFU rate is between 5% to 60% under missingness at random. From the results, it was observed that patients were missing due to both reasons such as they are feeling well, sick and also social issues such as migration. Several recommendations were made with other researchers who studied loss to follow-up events among patients receiving care(9). Such interventions include training to health care on the impact of loss to follow-up events and ways to handle, dealing with society stigma on sickle cell and engage patient community support groups to assist in improving engagement. Advocacy to patients on the importance of attending clinics even for days that they are feeling well can be one-way patient community can do to improve engagement. For families whose children have gone to boarding schools to inform the health care workers on that so that they can make follow-up in the respective schools. In addition, emphasis on newborn screening should be made and education to expecting parents on its importance so as to allow early detection which will result in better care. This study is not able to determine the survival for those lost to follow up, however, since this cohort was composed only of the HBSS genotype, this raises a concern. HBSS is associated with greater SCD related morbidity and mortality than the other subgroups (HbSC disease and HbSβ thalassemia)(13). Hydroxyurea was not the standard of care during the period of this cohort, and therefore there was no information on the level of fetal hemoglobin another predictor for survival. With this missing information, death remains a probable cause for LTFU in this cohort calling for further investigation on the fate of the patients that were lost to follow up.

Conclusion

Loss to follow-up is still a problem that requires strict measures to be enforced to minimize its effects. Necessary interventions are needed to be put into place to solve this such as the implementation of comprehensive care structures that include targeted education of caregivers, health care professionals and the beneficiaries such as the index child, to enhance long term follow up. The training education will provide means and techniques to undertake when patients are suspected to be to loss to follow- up. This could be a system that gives them alert based on historical values of some clinical and laboratory parameters collected by the cohort study. This study also describes LTFU that differs across the age groups and that requires address as more programs for standardizing care for patients with SCD are implemented in Tanzania. Newborn screening for SCD offers a crucial opportunity for intensifying the benefits of existing care to patients across the spectrum of ages by circumventing complications that would otherwise lead to an early death. Furthermore, advocacy to patients on the importance of attending clinics even for days that they are feeling well is very crucial.

Abbreviations

LTFU: Loss to follow-up; SCD: Sickle Cell Disease; SCP: Sickle Cell Patient; MNH: Muhimbili National Hospital; MUHAS: Muhimbili University of Health and Allied Sciences; MCV: Mean Corpuscular Volume; MCH: Mean Cell Hemoglobin; MCHC: Mean Corpuscular Hemoglobin Concentration; WBC:white blood cells; RBC: red blood cells and HB: hemoglobin concentration

Declarations

Ethics approval and consent to participate

The MSC study was approved by MUHAS ethical committee (MU/RP/AEC/VOL XI/33) and given permission by MNH. Written informed consent was obtained from all participants and for those under 18 a parent/ guardian consented and signed the consent on behalf of the patient.

Consent for publication

Not applicable

Availability of data and materials

The data of this study are available from the corresponding author on reasonable request

Competing interests

The authors declare that they have no competing interests.

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Author contributions

All authors have read and approved manuscript. BM and RZS designed the research study; UM performed statistical analysis and results interpretation; DK and JO did data collection and input but also took part in reviewing the manuscript.UM, RZS, FN, BM, SN, KM and JM contributed to writing and reviewing the manuscript. BM and RZS contribute equally to this manuscript.

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Appendix

Table 4. Univariate and multivariate cox proportional hazard model fitting results

	Univariate Analysis			Multivariate Analysis				
	Estimate	Hazard ratio	P-value	Estimate	Hazard ratio	P-value	lower 0.95	Upper 0.95
Sex (Male)	0.0819	1.0853	0.159					
Pre blood transfusion (Yes)	0.1076	1.1136	0.484					
Pre dactylitis (Yes)	-0.2414	0.7855	0.677					
Pre pain (Yes)	0.1135	1.1202	0.0669					
Pre chest (Yes)	0.1227	1.1305	0.415					
Pre convulsion (Yes)	-0.7094	0.4919	0.22					
Pre leg ulceration (Yes)	-0.9425	0.3897	0.103					
Pre priapism (Yes)	0.2814	1.325	0.574					
Pain (Yes)	-0.2834	0.7532	0.0005					
Fever (Yes)	0.2295	1.2579	0.0359					
Age group (5-17)	1.0212	2.7764	<2e-16	0.9624	2.6181	2.00E-16	2.2324	3.0705
Age group (0-4)	2.9007	18.1868	<2e-16	2.6602	14.2995	2.00E-16	11.0071	18.5768
Well today (Yes)	0.1839	1.2019	0.0027	0.1249	1.1331	0.0495	1.0003	1.2837
Mean corpuscular volume (fL)	-0.0049	0.9951	0.0925					
Mean cell hemoglobin (pg)	-0.0369	0.9638	3.26E-06					
Mean corpuscular hemoglobin concentration (g/dL)	-0.0812	0.922	1.43E-10					
White blood cells (10^3/uL)	0.0349	1.0355	8.74E-15	0.0157	1.0158	0.0074	1.0042	1.0276
Red blood cells (10^6/uL)	0.0421	1.043	0.28					
Mean platelet volume (fL)	-0.1372	0.8718	4.58E-06					
Hemoglobin concentration (g/dL)	-0.0371	0.9635	0.0753					
Diastolic blood	-0.0047	0.9953	0.156					

pressure								
Systolic blood pressure	-0.0183	0.9819	1.29E-13	-0.0078	0.9922	0.0022	9872	0.9972
Temperature	0.109	1.1151	0.0485					
Hematocrit (%)	0.0034	1.0034	0.618	0.0235	1.0238	0.0039	1.0076	1.0404

Variables starting with “Pre” were attributes that were collected from patients asking on any episodes that they faced since their last clinic that required OPD attendance or admission.

Fever this attribute explains if one has fever (1) or does not have(0); painful this attribute says if one has painful episodes (1) or not (0) and well_today states if one is well (0) or not well

Table 5. Cox proportional test results on assumptions of proportionality

	rho	chisq	p-value
White blood cells (10^3 u/L)	-0.0007	5.78E-04	0.9808
Hematocrit (%)	0.0521	3.13E+00	0.0770
Well today (Yes)	-0.0431	2.16E+00	0.1420
Age group (5-17)	-0.0455	2.13E+00	0.1445
Age group (0-4)	-0.0440	2.16E+00	0.1420
mch:time_group(0-2050 days)	-0.0106	1.33E-01	0.7158
mch:time_group(>2050)	0.0571	4.52E+00	0.0335
mcv:time_group(0-2050 days)	0.0042	2.07E-02	0.8855
mcv:time_group(>2050)	-0.0467	3.24E+00	0.0719
GLOBAL	NA	1.50E+01	0.1312

Figures

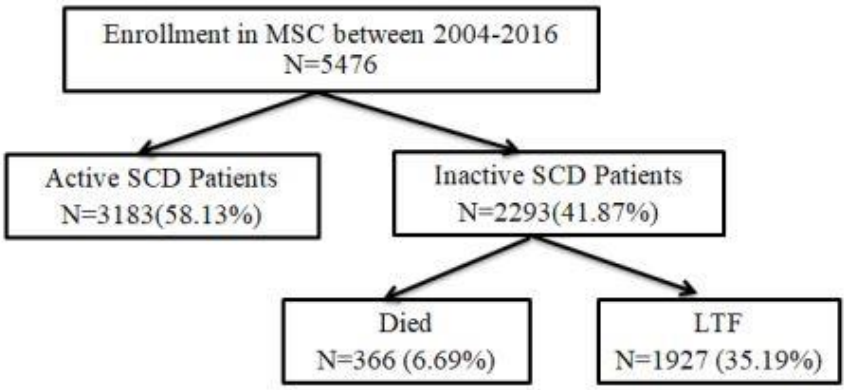

Figure 1

Muhimbili Sickle Cell Cohort description of the data used for loss to follow-up analysis.

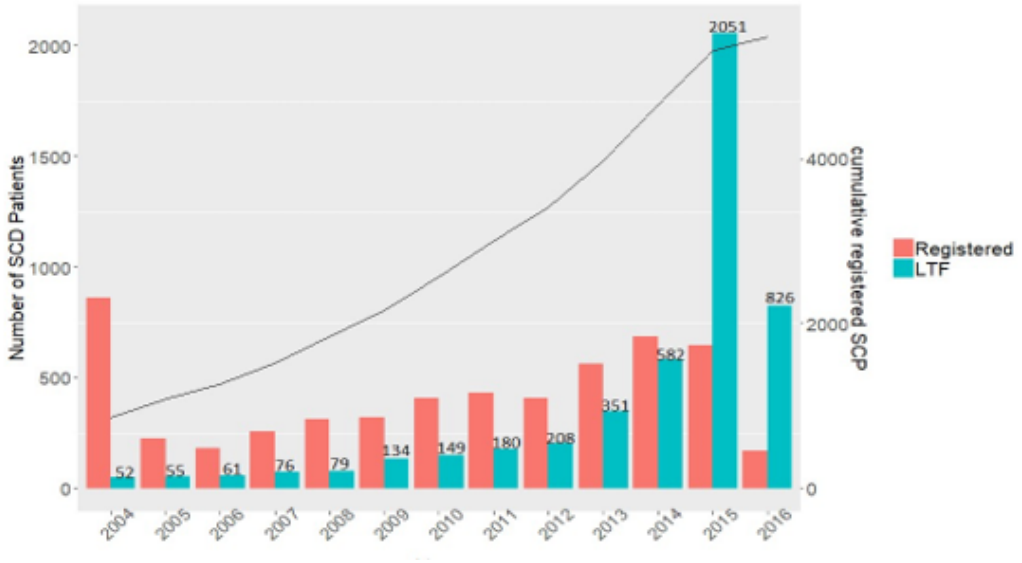

Figure 2

Annual trend of enrollment and loss to follow-up events.

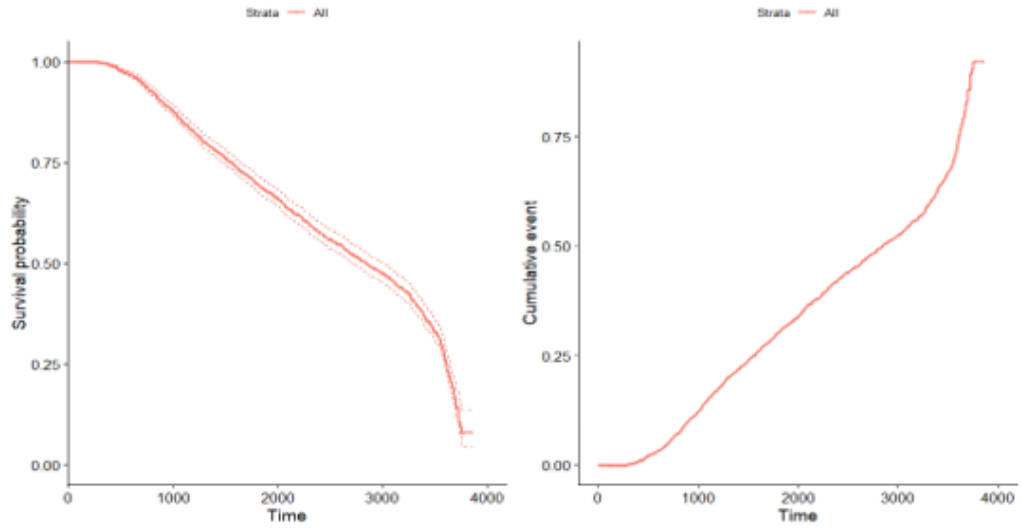

Figure 3

Survival probabilities and cumulative loss to follow-up events with time among SCD patients.

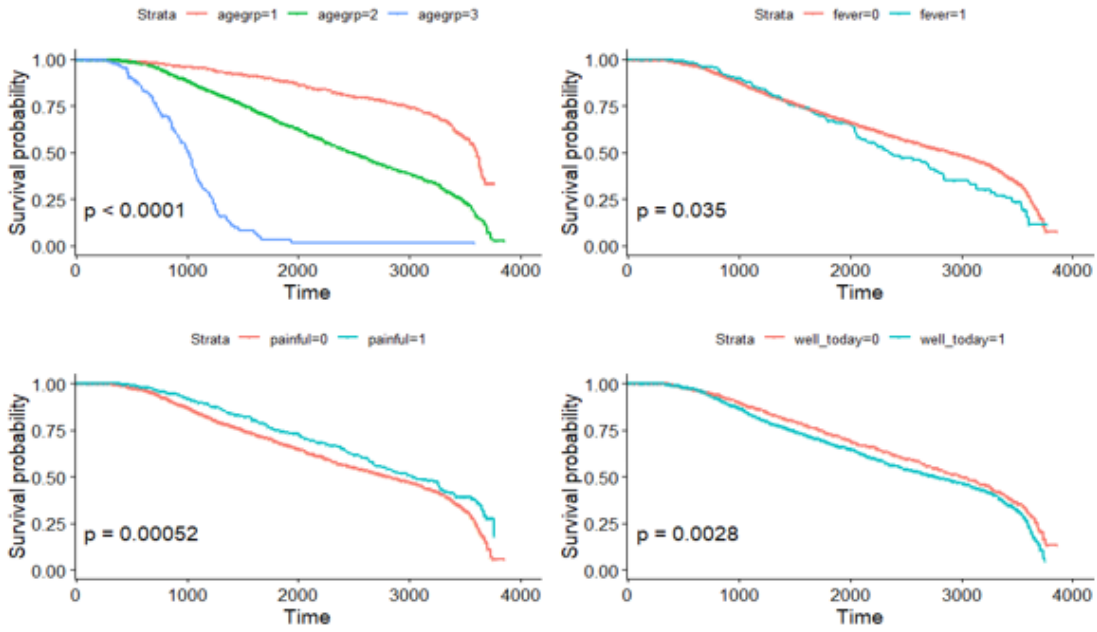

Figure 4

Survival probabilities for different group's attributes in our data.