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Assessing Medication Adherence and Complications in Children Under Five with Sickle Cell Disease at Hoima Regional Referral Hospital

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ABSTRACT

Sickle cell disease (SCD) is a group of inherited haemoglobin disorders with abnormal sickle haemoglobin in red blood cells. Sickle cell anemia, the most common and severe form, results from homozygous inheritance of sickle haemoglobin from both parents. A study was conducted at Hoima Regional Referral Hospital to determine medication adherence and complications among under-fives with SCD. The majority of children were over three years old (48.2%), with over half being females (58.2%). The majority of parents or care takers were over forty years old (48.2%). The study found that poor adherence to sickle cell medication was most common in under five children whose mothers or caregivers were illiterate and of young age. The study aimed to identify factors associated with medication adherence among these children and to provide specific attention to this group of patients.

Keywords: medication adherence, complications, sickle cell disease

INTRODUCTION

Sickle cell disease (SCD) refers to a group of inherited haemoglobin disorders characterized by a predominance of abnormal sickle haemoglobin in red blood cells [1-3]. The first clinical description of SCD was made more than 100 years ago [4-7], but the discovery of the molecular basis of SCD was a landmark in molecular medicine [8-10]. Several decades of observational studies and therapeutic trials have contributed to a greater understanding of the pathophysiology and management of SCD [11-14]. Sickle cell disease is a group of genetic conditions which result from the inheritance of the sickle cell gene either hemizygously or as a double heterozygote with another interacting gene [15-18]. Sickle cell anemia, which results from homozygous inheritance of sickle haemoglobin from both parents, is the most common and severe form of SCD [19-22], accounting for approximately 60% to 65% of all cases of SCD. Sickle cell anemia results from a point mutation that leads to the replacement of hydrophilic glutamic acid by hydrophobic valine at the sixth position of the beta (β) globin chain [23-25]. When deoxygenated, sickle haemoglobin undergoes a conformational change that promotes intracellular polymerization, leading to distortion of the normal biconcave red blood cell into the distinctive and pathological crescent shape [26-27]. This consequently manifests as multisystem symptoms, recurrent vaso-occlusion and organ damage, causing substantial morbidity and early mortality [28-30]. Before 1 year of age, affected children begin to have anaemia, pain, stroke, retinopathy, and chronic damage affecting the spleen, lungs, kidney, and major joints [31-35].

METHODOLOGY

Study design

A hospital-based cross-sectional study design was used to determine the prevalence of medication adherence, and factors associated with medication adherence among under-fives with sickle cell disease at Hoima Regional Referral Hospital.

Study site

The study was be carried out at Hoima Regional Referral Hospital located in Hoima district.

Target population

This study targeted children aged less than five years with sickle cell disease.

Study population

Children aged less than five years with sickle cell disease who were attending the sickle cell out-patient clinic of Hoima regional referral hospital during the time of data collection were involved.

Study duration

The study was conducted for a period of three (3) months from February to April 2020.

Sample size determination

The sample size was determined, using Fischer's et al 1990 formula. However, at least 100 samples were selected during data collection period.

$\mathbf{N=Z^2PQ/D^2}$

Where; **N** is the desired sample size

Z is the standard normal deviation taken as 1.96 at a confidence interval of 95%

P is the proportion of the target population estimated to have similar characteristics = 7% (Fischer's et al, 1990)

D is the degree of accuracy= 0.05

Q= (1-P) which is the population without the desired characteristics. Therefore; $\mathbf{N}= 1.96^2$ X0.07 (1-0.07)/ $(0.05)^2$= 100

Selection criteria

Inclusion criteria

Children aged less than 5 years with sickle cell disease who were attending the out-patient department of Hoima regional referral hospital during the time of data collection.

Exclusion criteria

Under-fives presumed to have sickle cell disease but with no positive hemoglobin electrophoresis results.

Sampling technique

Children who meet the inclusion criteria were consecutively enrolled into the study until when the desired sample size was attained.

Data collection procedure

An introductory letter was sought from the administration of Kampala International University western campus to carry out the study and it was then taken to research ethical committee of KIU to allow conduct research, and then the two letters were presented to the executive director Hoima regional referral hospital to grant permission to conduct research in the hospital. The researcher then informed the Records department the purpose of the study and what use was to be made out of the data.

Data collection

Data was collected in form of a table which had the following columns; file number, age, sex, date of admission/visit, diagnosis of malaria, anemia, infections, stoke, and deaths. Data from completed questionnaires were arranged, summarized and entered using the statistical computer software package, Microsoft Excel 2019. The data was cleaned, checked for errors and corrected, then imported to STATA version 13 (Statacorp, College station, USA) for analysis by objective, with the guidance of a biostactician. Caretaker and child characteristics were described using means or median for continuous variables and proportions for categorical variables, and presented in tables and graphs.

Ethical considerations

For the study to be ethical, the following were considered;

Institutional consent

Ethical approval was sought from the research ethics committee (REC) of Kampala International University, western campus. Permission to execute the study was sought from the director of Hoima Regional Referral Hospital. Permission to pre-test the questionnaires was sought from the medical superintendent of Virika hospital.

Informed consent

Informed consent was sought from each caregiver and the purpose of the study was well explained to the participants in a language they understand before they answer the questions. In order to participate in the study, the caregiver was also requested to sign a written informed consent document or use a thumb print for those who do not know

how to write. A copy of the signed consent form was given to the participant and another copy kept by the principal investigator. The consent forms were in both English and Runyoro, and the participants had the right to decline to participate or withdraw from the study at any time if they would wish.

RESULTS

Table 1: Socio-demographics of the under five children with sickle cell disease

VARIABLE		FREQUENCY	PERCENTAGE (%)
AGE	1 year	11	10%
	2 years	22	20%
	3 years	24	21.8%
	4 years	53	48.2%
sex	Male	46	41.8%
	Female	64	58.2%
BIRTH ORDER	1	22	20%
	2	64	58.2%
	3	24	21.8%

Mothers and care takers of 110 children below five years with sickle cells attending at HRRH were involved in the research. Majority of children were over 3 years 53(48.2%) while others were 2 years and 3 years 20% and 21.8% respectively. Over half of the children were females 64(58.2%) and their most birth order was 2nd (58.2%). Table 1

Table 2: Caregivers' Socio-demographics

VARIABLE	FREQUENCY	PERCENTAGE (%)
EDUCATION		
No formal education	35	31.8%
Primary	27	24.6%
Secondary	34	30.9%
Tertiary	14	12.7%
MOTHERS AGE		
20 and below years	11	10%
21-30 years	22	20%
31-40 years	24	21.8%
Above 40 years	53	48.2%

Majority of parents or care takers 48.2% were over forty years. Twenty one percent (21%) and 20% were in age group 31-40 years and 21-30 years respectively. Less than half of parents had attained up to secondary level of education [Secondary; 30.9%, Primary; 24.6% & Non formal education; 31.8%]. Only 12.7% had reached a tertiary level of education. Majority of children 80.9% had ever received Pneumococcal vaccine (PCV). However about 19.1% reported that their children never received Pneumococcal vaccine (PCV). About 71% of children were on medication for sickle cell with 29% not on medication at the time of study. (Figure 1). However, among children who were on medication, 43% and 52% reported always and sometimes using medicine respectively. Children were reported on medication involving Penicillin V, Folic acid, Fansidar, and Hydroxyurea. (Figure 4.2). Over half (57%) of children were using Penicillin V while all children who were on medication were using Folic acid. Less than half 43.6% and 26.9% who were on medication were using Fansidar and Hydroxyurea respectively. Among children who were on penicillin V medication, 33.3% & 75.6% had used for 1-3 months and 4-6 months respectively. Additionally, for children using Folic acid, 70% had used for over 6 months.

Figure 1: Distribution of current medical use among under-fives with sickle cell disease

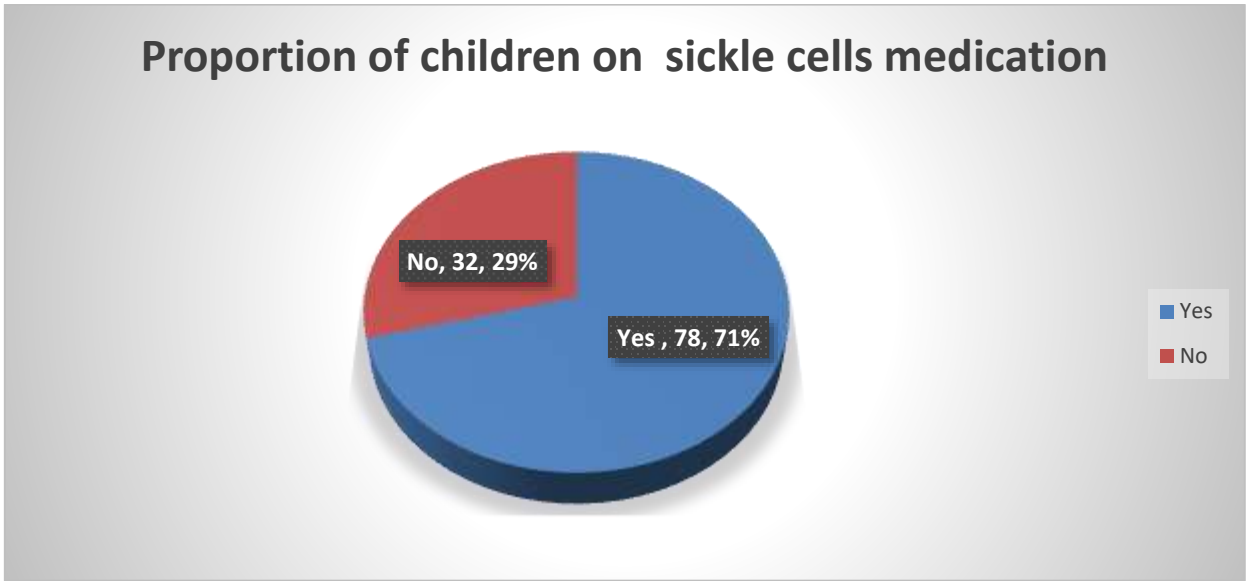

Figure 2: Number of children using Penicillin V, Fansidar, Folic acid and Hydroxyurea.

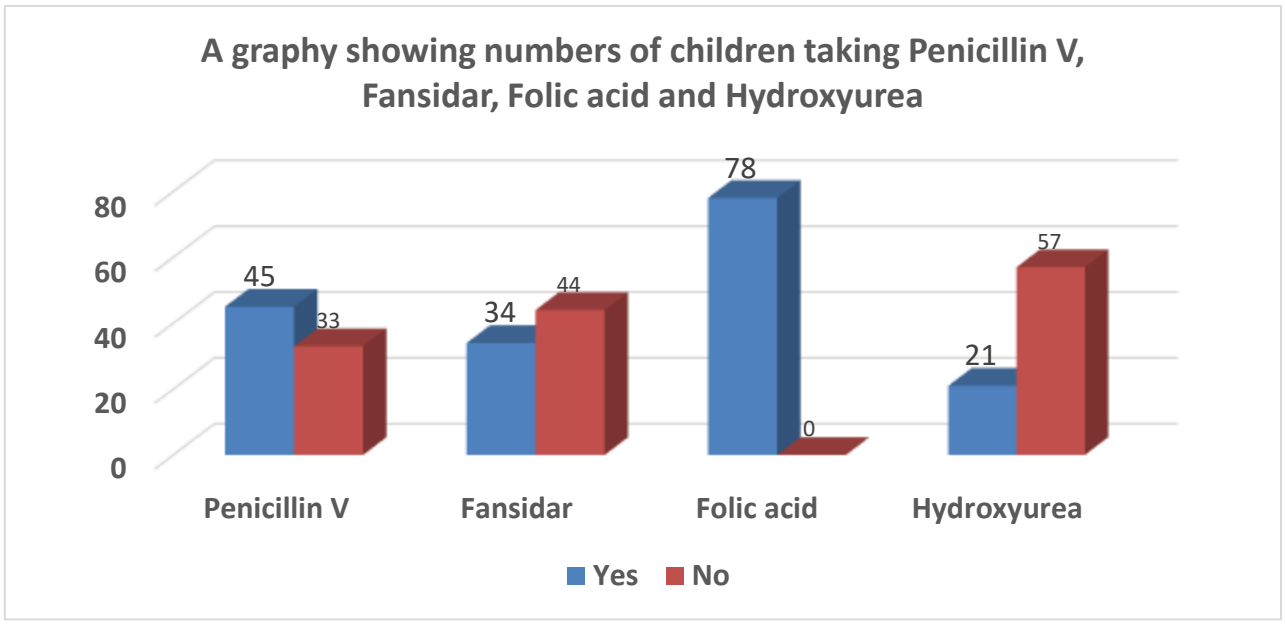

Table 3: Prevalence of adherence to routine medication and vaccinations

VARIABLE		FREQUENCY	PERCENTAGE (%)
EVER VACCINATED WITH PCV	Yes	89	80.9%
	No	21	19.1%
Children currently taking any medication	Yes	78	70.9%
	No	32	29.1%
Medicine currently being taken			
Penicillin V	Yes	45	57.7%
	No	33	42.3%
Folic acid	Yes	78	100%
	No	0	0%
Fansidar	Yes	34	43.6%
	No	44	56.4%
Hydroxyurea	Yes	21	26.9%
	No	57	73.1%
PERIOD SPENT ON MEDICATION			
Penicillin V	1-3 months	13	33.3%
	4-6 months	21	75.6%
	More than 6 months	11	24.4%
Folic acid	1-3 months	2	2.6%
	4-6 months	21	26.9%
	More than 6 months	55	70.5%
Fansidar	1-3 months	34	100%
Hydroxyurea	3-6 months	21	100%
OFTNESS IN TAKING MEDICATION	Always	35	47.3%
	Sometimes	39	52.7%

Over eighty percent of the under-fives reported to have been vaccinated with PCV and 21(19.1%) were not vaccinated. Of those who were not vaccinated, their caregivers were non-literate with no formal education and primary level of education accounting for 9.2% and 90% respectively. Children whose caregivers reported being illiterate were more likely not to be vaccinated with PCV and this was significant with $p<0.001$. Additionally, 70.9% of the children with sickle cell disease were reported to be taking some medications and the rest were not taking any. Of those who were not taking, majority of them had their caregivers lacking formal education (34.4%) and primary level of education (50%). The under five children with sickle cell disease whose caregivers were illiterate were more likely to miss of fail to take medications and this was significant at $p<0.001$. Furthermore, of those under-fives who were not taking Penicillin V, majority of their caregivers had no formal education (59.1%) and 15.9% stopped in primary, $p<0.001$. Additionally, under-fives who were not taking Folic acid, Fansidar and Hydroxyurea had their caregivers lacking formal education and others stopped in primary illiterate and these accounted for [36.4%,63.4%, $p<0.001$], [47%,12. %, $p<0.001$] and [41.8%,24.1%, $p<0.001$] respectively. Over half of the under-fives reported taking medication always and 47.7% reported taking medication sometimes. The non-literate care givers (no formal education and primary) were more likely to not fully give medication to their under-five with sickle cell compared to the literates (secondary and tertiary) accounting for [48.8%, 19.5% Vs 26.8%,4.9%, $p=0.001$] respectively as presented in table 4

Table 4: Education and factors associated to sickle cell medication adherence among Under-fives

			Care taker's level of education				P-value
			No formal education (%)	Primary (%)	Secondary (%)	Tertiary (%)	
Child ever vaccinated with PCV	Yes		33(37.1)	8(9)	34(38.2)	14(15.7)	P<0.001
	No		2(9.2)	19(90)	0(0)	0(0)	
Children currently taking any medication	Yes		24(30.7)	11(14.1)	32(41)	11(14.1)	P<0.001
	No		11(34.4)	16(50)	2(6.3)	3(9.4)	
Medicine currently being taken	Penicillin V	Yes	7(12.5)	12(21.4)	34(60.7)	3(5.4)	P<0.001
		No	26(59.1)	7(15.9)	0(0)	11(25)	
	Folic acid	Yes	29(32.6)	12(13.5)	34(38.2)	14(15.7)	P<0.001
		No	4(36.4)	7(63.4)	0(0)	0(0)	
	Fansidar	Yes	2(5.9)	11(32.4)	21(61.8)	0(0)	P<0.001
		No	31(47)	8(12.1)	13(19.7)	14(21.2)	
	Hydroxyurea	Yes	0(0)	0(0)	21(100)	0(0)	P<0.001
		No	33(41.8)	19(24.1)	13(16.5)	14(17.7)	
OFTNESS IN TAKING MEDICATION	Always		7(15.7)	5(11.1)	23(51.1)	10(22.2)	P=0.001
	Sometimes		20(48.8)	8(19.5)	11(26.8)	2(4.9)	

Majority (95.2%) of the under-fives who were not vaccinated with PCV had young caregivers between 20-30 years. There was a likelihood of under-fives with sickle cell not being vaccinated with PCV given that their caregivers being of young age compared to the older caregivers [95.2% Vs 4.8%, 0%, p<0.001]. Additionally, young caregivers were more likely to have their children with sickle cell disease stay without taking medication compared to the older caregivers (31-40 years and above 40 years) [65.6% Vs34.4%,0%, p=0.024]. Furthermore, young caretakers were more likely to give medications to their under-fives rarely (sometimes) other than always compared to the older caregivers [43.9% Vs 34.2%, 22%, p=0.002] Table 5

Over eighty five percent of the children who were not immunized with PCV vaccine were of birth order 1 and only 14% were of birth order 2. This was statistically significant at p<0.001. Majority (65.6%) of the children who reported not taking sickle cell medications were of birth order 2 and 34.4% were of birth order 1, none was of birth order 3. Birth order 2 (56.1%) under-fives were more likely not to always take medication compared to birth order 1 (24.4%) children and birth order 3 (19.5%) children, p=0.024. Table 5 Sex of the child and factors associated with adherence to sickle cell medication among under-fives.The female under-fives with sickle cell disease were more likely not to be vaccinated with PCV compared to the males (100% Vs 0%, p<0.001) respectively. Additionally, the female under-fives with sickle cell disease were more likely not to be given sickle cell medication compared to the males (65.6% Vs 34.4%) respectively. However, this was not statistically significant with P=0.311. Furthermore, majority (58.5%) of the children who rarely (sometimes) receive sickle cell medication were females compare to males (41.5%) and there was no statistical significance with p=0.192.

Table 5: Caretaker's age, child's birth order, sex of the child and factors associated with adherence to sickle cell medication among under-fives attending HRRH

		Care takers' Age			Birth order			Sex of the child	
		20-30 years n(%)	31-40 years n (%)	Above 40 years n (%)	1 n (%)	2 n (%)	3 n (%)	Male n (%)	Female n (%)
	P-value	P<0.001			P<0.001			P<0.001	
Child ever vaccinated with PCV	Yes	33(37.1)	47(52.8)	9(10.1)	8(9)	54(64)	24(27)	46(51.7)	43(48.3)
	No	20(95.2)	1(4.8)	0(0)	18(85.7)	3(14)	0(0)	0(0)	21(100)
		P=0.024			P=0.001			P=0.311	
Children currently taking any medication	Yes	27(34.6)	42(53.8)	9(11.5)	11(14.1)	43(55.1)	24(30.8)	35(44.9)	43(55.1)
	No	21(65.6)	11(34.4)	0(0)	11(34.4)	21(65.6)	0(0)	11(34.4)	21(65.6)
		P=0.002			P=0.024			P=0.192	
OFTNESS IN TAKING MEDICATION	Always	18(40)	27(60)	0(0)	2(4.4)	29(64.4)	14(31.1)	25(55.6)	20(44.4)
	Sometimes	18(43.9)	14(34.2)	9(22)	10(24.4)	23(56.1)	8(19.5)	17(41.5)	24(58.5)

Majority of the under-fives with sickle cell disease were also reported to be affected by Asthma 53(48.3%) and had chronic pain 56(50.9%). None had HIV and heart disease. Figure 4.3

Furthermore, all children were reported to be affected by other medical complications such as Painful crisis 56(50.9%), Acute chest syndrome 66(60%), Aplastic crisis 86(78.2%), **Severe** anemia 43(39.1%), Stroke 88(80%) and infections 65(59.1%). None of the children was reported to be facing splenic sequestration complications. All caregivers reported no history of other children with sickle cell disease. Table

Figure 3: Graphical presentation of other chronic medications suffered by the under-fives with sickle cell disease attending HRRH

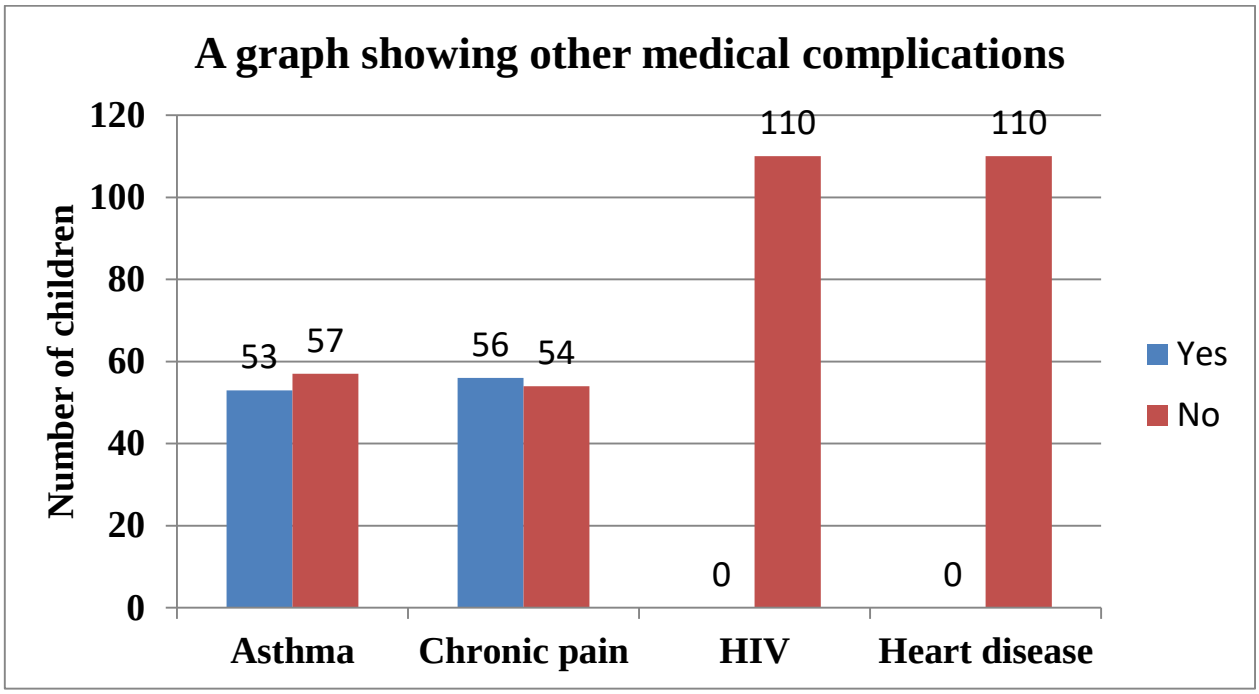

Table 6: Sickle cell medical complications among under-fives attending HRRH

Variable	**Frequency**	
Other chronic medical problems	**Yes** **n (%)**	**No** **n (%)**
Asthma	53(48.3)	57(51.8)
Chronic pain	56(50.9)	54(49.1)
HIV	0(0)	110(0)
Heart disease	0(0)	110(0)
Any medical complication	110 (100)	0(0)
Nature of medical complication		
Painful crisis	56 (50.9)	54(49.1)
Acute chest syndrome	66(60)	44(40)
Splenic sequestration	0(0)	110(100)
Aplastic crisis	86(78.2)	24(21.8)
Severe anaemia (necessitating blood transfusion)	43(39.1)	67(60.9)
Stroke	88(80)	22(20)
Priapism	0(0)	108(100)
Infections	65(59.1)	45(40.9)
Other child with sickle cell disease	0(0)	110(100)

DISCUSSION

The study had an overall aim of determining medication adherence and complications among under-fives with sickle cell disease attending Hoima Regional Referral Hospital. The study found out that majority of the under-fives had been vaccinated with PCV which is a good adherence. Lack of formal education and or having stopped in primary, young mothers and caregivers of under-fives, being of birth order one and female gender were the leading factors for failure to vaccine PCV among under-fives. Furthermore, penicillin V was found out to be the commonest used treatment among under-fives with sickle cell disorder. However, its usage was too low since a few under-fives reported to have used it for only one to three months other than reasonable period (four to six months). The study also found out that failure to provide medication to under-five children with sickle cell disease is possibly as a result of poor education of the caregivers, birth order of the child and caregiver's age [30-31]. The gender of the child was not associated to failure to give medication to the under-fives. Poor medication adherence or failure to give medication as prescribed (giving medication sometimes) was found significant with young caregivers age, children of birth order one and female under-fives [32-35].

CONCLUSION

As poor adherence to sickle cell medication was most frequently encountered in under five children whose mothers or caregivers were illiterate and of young age, particular attention should be given to this group of patients.

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