Original Article

The relation between regular outpatient follow-up and frequency of emergency department visits in sickle cell pediatric patients

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ABSTRACT

الأهداف: تقييم العلاقة بين المتابعة في العيادات الخارجية (OPD) وتواتر زيارات الطوارئ لدى أطفال مرضى الأنيميا المنجلية (SCD).

المنهجية: أجريت دراسة حشدية رجعية بالملاحظة على 247 مريضاً من الأطفال المصابين بالأنيميا المنجلية في مستشفى الولادة والأطفال، قسم طب الأطفال في المدينة المنورة، المملكة العربية السعودية. تراوحت فترة الدراسة من عام 2016م إلى 2018م، حيث تم جمع البيانات من نظام التسجيل الإلكتروني واشتملت على التركيبة السكانية للمرضى، والأدوية المصروفة لهم، وعدد زيارات الطوارئ، وعدد العيادات الخارجية والتغيب عنها. تم جمع وتحليل البيانات إحصائياً بواسطة برنامج Excel وبرنامج SPSS على التوالي، وتم تطبيق معامل ارتباط بيرسون، والإنحدار الخطي، واختبار–T لعينتين مستقلتين.

النتائج: لم يكن هناك دلالة احصائية (p=0.07) بين التردد على الطوارئ والعيادات الخارجية، ولكن اتضحت دلالة احصائية بين التردد على الطوارئ وعدد زيارات العيادات المتغيب عنها (p<0.001) فيمكن توقع التردد على الطوارئ من خلال عدد الزيارات الفائتة للعيادات الخارجية باستخدام الانحدار الخطي بحيث أن التغيب عن زيارة العيادة لمرة واحدة قد يساهم بزيادة التردد على الطوارئ 1.92 زيارة، بالإضافة إلى أنه لوحظ زيادة في عدد زيارات الطوارئ لعينة الدراسة هذه مقارنة بدراسات أخرى مع زيادة في الاعتماد على الطوارئ بمعدل 43%.

الخلاصة: وجدت الدراسة أن المتابعة في العيادات الخارجية قد تساهم في تحسين السيطرة على المرض حيث وجدت علاقة طردية بين التردد على الطوارئ والتغيب عن العيادات الخارجية مما أدى الى زيادة الاعتماد على الطوارئ بشكل كبير.

Objectives: To evaluate the relationship between the frequency of ED visits and outpatient department (OPD) follow-up in sickle cell disease (SCD) pediatric patients.

Methods: A retrospective cohort study included 247 SCD pediatric patients between January 2016 and December 2018 at the Maternity and Children Hospital, Department of Pediatrics, Al Medinah Al Munawarah, Saudi Arabia. Data were extracted from electronic medical record system; patient demographics, medications, frequency of emergency department (ED) and OPD visits. Pearson correlation coefficient, linear regression and independent sample t-test were applied.

Results: There was no significant correlation (95% CI [-0.013- 0.233]; p=0.07) between the frequency of ED and OPD visits. However, a significant correlation was found between ED visits and missed OPD appointments. Thus, linear regression was applied and indicated that one missed OPD appointment is associated with 1.92 ED visits, (95% CI: 0.19-0.42; p<0.001). Also, a higher rate of ED visits was observed when compared with other studies, with a high ED reliance of 43%.

Conclusion: This study found that regular OPD visits could improve SCD management, as a directly proportional relationship between the frequency of ED visits and missed OPD appointments were found, along with high ED reliance.

Keywords: sickle cell disease, emergency department, out-patient department

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Sickle cell disease (SCD) is an autosomal recessive blood disorder that results from a mutation in the beta-globin chain of the hemoglobin molecule. Glutamic acid is substituted with valine at the position of β6 chain, leading to polymerization of hemoglobin and production of hemoglobin S (HbS) whenever it is deoxygenated.[1] Across the world, sickle cell disease is the most common inherited blood disorder, with a wide variability in prevalence among different ethnic and racial groups.[2,3] The worldwide incidence of SCD is approximately 200,000 per year, with more than half of the cases in Sub-Saharan Africa.[4] In Saudi Arabia, a high prevalence rate of 49.6% (45.8% for the trait and 3.8% for the disease) was reported in 2015.[5] This could be attributed to the high percentage of consanguineous marriages around the country (57.7%), and an even higher percentage in rural areas (80%). This is considered as a major challenge to control SCD in Saudi Arabia.[5,6]

The pathogenesis of SCD starts when HbS becomes deoxygenated and polymerized under the effect of certain risk factors, such as: stress, hypoxia, acidosis, and so on. This produces fragile sickle-shaped red blood cells (RBCs).[6] Subsequently, microvascular circulation is occluded by these sickled RBCs leading to tissue ischemia, infarction, and release of inflammatory mediators, resulting in severe, acute painful episodes. These episodes are known as vaso-occlusive episode (VOEs) that can affect any organs such as bones, muscles, mesentery, spleen, and the like.[4]

Sickle cell disease has significantly shortened the life expectancy in children as a result of early complications during childhood, such as, poor development and failure to thrive, as well as multiple organ damage due to repeated VOEs. Therefore, the high prevalence of SCD and its complications and evidence from other countries would suggest that patients with SCD have high utilization of medical resources.[7,8]

Management programs for pediatric patients with SCD are highly demanding, including acute care management (VOEs), routine prevention (growth and development monitoring, vaccination, and transcranial doppler ultrasound annual monitoring), treatment of disease complications, blood transfusion therapy, and hydroxyurea therapy.[4] In addition, folic acid is prescribed to prevent bone marrow aplasia, as well as daily prophylactic penicillin to prevent pneumococcal infection.[9]

Major part of SCD patient's management program is done during (out-patient department) OPD visits. Thus, missing hematology OPD appointments lead to loss of OPD advantages, such as patient and parental education on how to manage pain episode at home, how to avoid vaso-occlusive crises, recognize early signs of complications, when to give prophylactic antibiotic, and physical assessment skills (spleen palpation), as well as screening for complications, lab tests, immunization, and growth monitoring.[9] Moreover, a previous study showed that higher parental education was related to compliance with OPD for routine disease management instead of acute management of the disease.[10] Another study carried out in Riyadh, Saudi Arabia showed that missed OPD appointments were an indicator of poor compliance with medications. In contrast, parents who were compliant with OPD appointments were more compliant with their children's medications.[11]

Several studies have shown the importance of OPD visits in disease management and acute crisis. A study in the United States showed that access to OPD visits plays a significant role in the frequency of emergency department (ED) utilization.[12] Another study found that follow -up in OPD within 14 days after hospitalization due to sickle cell crises has significantly decreased the 30 and 14 day rehospitalization rates.[13] Note that the high utilization of ED visits can be decreased by improvement of patient education and continuity of care with an attending physician at OPD.[14,15]

Measures of ED utilization has traditionally focused on resources used and the total number of ED visits. These measures are informative on ED use specifically, but they do not reflect any information on how these visits correlate with total health care usage. In contrast, emergency department reliance (EDR) measures the use of the ED in relation to utilization of all health care services, to distinguish between patients with frequent ED visits due to the increased need of care, from patients without adequate OPD follow-up.[16]

There are no similar studies carried out in Saudi Arabia that correlate OPD follow-up and the frequency of ED visits for SCD pediatric patients. Thus, the aim of this study is to investigate the relationship between OPD follow-up and the frequency of ED visits in SCD pediatric patients, and how missing hematology OPD appointments might influence the utilization of ED in Al Madinah Al Munawarah, Saudi Arabia. The hypothesis of this study is that regular OPD visits can decrease the reliance on ED in children with SCD.

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Methods. The study has been approved by the Institutional Review Board and the Taibah University Scientific Research Ethics Committee. A retrospective cohort study was conducted to analyze the relationship between frequency of OPD visits and frequency of ED visits in sickle-cell pediatric patients at Maternity and Children's Hospital (MCH), Department of Pediatrics, Al Medinah Al Munawarah, Saudi Arabia. Maternity and Children's Hospital is considered the main hospital that provides secondary healthcare for SCD patients in the Al Medinah Al Munawarah, Saudi Arabia. The study period was between January 2016 and December 2018.

All patients with approved diagnosis of SCA and patients that were followed regularly for the whole 3-year period time in OPD were included. Moreover, patients who did not follow up in the hematology OPD but presented in the ED more than 2 times during study duration were included. As well as patients who had provided hematology OPD appointments for follow up, but they didn't present in OPD were included. However, patients with SCA trait, insufficient data, or had zero hematology OPD visits were excluded.

Patients were divided into 2 age groups: children (4-9 years old) and adolescents (10-18 years old) based on the first clinical encounter. The following data were collected from the electronic medical record system (Medic Plus): age, gender, prescribed medications; hydroxyurea and folic acid, frequency of ED visits, frequency of hematology OPD visits, and missed hematology OPD appointments (patients who had provided OPD appointments for follow up but they didn't show up)

Statistical analysis. Data collection and statistical analysis were performed by Microsoft Excel version 16.16.27 and the Statistical Package for Social Sciences for Windows, version 21.0. (IBM Corp, Armonk, NY. USA). Descriptive statistics summarized the following variables: age, gender, comorbidity; prescribed hydroxyurea and folic acid. The relationship between OPD and ED visits, missed hematology OPD appointments and ED visits; was analyzed by the Pearson correlation coefficient test. Linear regression was applied to predict the frequency of ED visits from missed hematology OPD appointments. Independent sample t-test was performed to evaluate the difference between the mean of ED and OPD visits across different variables: gender, comorbidity, hydroxyurea and folic acid. P-value <0.05 was considered significant.

Percentage and number of ED visitors, OPD visitors and frequent ED utilizers (≥2 ED visits) were identified. EDR which is the total of ED visits divided by the total ambulatory visits (hematology and non-hematology OPD visits + ED visits) was calculated. EDR greater than 0.33 was considered high.[16,17]

Results. The study population was a total of 247 SCD patients presented to the ED or OPD between January 2016 and December 2018. Patients were divided into 2 age groups according to the first clinical encounter during the study period: 103 children (4-9 years) and 144 adolescents (10-18 years). Demographics (age, gender, comorbidity, and medication) are illustrated in Table 1. Approximately, 22% of patients had comorbidity (asthma, epilepsy, cardiomyopathy, so on). In addition, 78% of the patients were treated with folic acid, while only 23% were on hydroxyurea.

During the study, there were 1888 total ED visits (mean=7.64, SD=9), 1233 total OPD visits (mean=4.99, SD=4.9) and 375 total missed hematology OPD appointments (mean=1.52, SD=1.4). Number of ED visitors among the study population was 210 patients (85% of study population) and the number of patients who considered frequent ED visitors (have ≥2 ED visits) was 186 (88.5% of ED visitors). Moreover, the number of patients who visited OPD among the study population was 222 (89.9% of study population). The average ED visits per patient per year was 2.93 for

Table 1 - Demographics and medication.

Demographics	n	(%)
Age group		
Adolescent	144	(58.3)
Children	103	(41.7)
Total	247	(100)
Gender		
Male	122	(49.4)
Female	125	(50.6)
Total	247	(100)
Comorbidity		
Yes	55	(22.3)
No	192	(77.7)
Total	147	(100)
Prophylactic medication		
Hydroxyurea		
Yes	58	(23.5)
No	189	(76.5)
Total	247	(100)
Folic acid		
Yes	192	(77.7)
No	55	(22.3)
Total	247	(100)

ages 4-9 years, and 2.27 for ages 10-18 years.

Emergency department reliance was calculated via the following formula: total ED visits/[total OPD visits (hematology and non-hematology clinics) + ED visits] for each patient, the mean EDR found to be 0.43, which is higher than the cut-value 0.33.

There was no significant correlation (95% CI [-0.13, 0.233]; p=0.07) between the frequency of ED visits and the frequency of OPD visits. (Table 2)

There was a significant correlation between ED visits and missed hematology OPD appointments (95% CI [0.188- 0.415]; p<0.001). A simple linear regression was calculated to predict the frequency of expected ED visits based on the number of missed hematology OPD appointments. Thus, we can estimate the expected frequency of ED visits from missed appointments by the following equation: frequency of ED visits=4.728 + 1.920 x missed hematology clinic appointments, (R=0.31, R^2=0.93, adjusted R^2=0.9). The equation showed a directly proportional relationship between the frequency of ED visits and missed hematology OPD appointments, in which one missed appointment contributed to 1.92 ED visits. (Figure 1)

There was no significant difference found between ED visits among patients treated with hydroxyurea and did not treat with hydroxyurea (95% CI [-1.1-4.1]; p=0.270). Similarly, no significant difference was found between the mean of ED visits among patients treated with folic acid and did not treat with folic acid (95% CI [-0.5- 4.9]; p=0.1). A higher frequency of ED visits was noted in patients with comorbidity and without comorbidity (95% CI [6.8-11.8], p=0.000)(Table 3).

Table 2 - Correlations between frequency of ED visits with frequency of OPD visits and missed OPD appointments.

Frequency of OPD visit for hematology clinics	Frequency of ED visit
Pearson correlation	0.112
Significant (2-tailed)	0.079
Confidence interval	[-0.013, 0.233]
Number of patients	247
Frequency of missed hematology clinic appointments	
Pearson correlation	0.306
Significant (2-tailed)	0.001
Confidence interval	[0.188, 0.415]
Number of patients	247

No significant correlation (95% CI [-0.13, 0.233]; p=0.07) between frequency of emergency department (ED) visit and frequency of OPD visit. Significant correlation (95% CI [0.188- 0.415]; p<0.001) between frequency of ED visits and frequency of missed outpatient department (OPD) appointments.

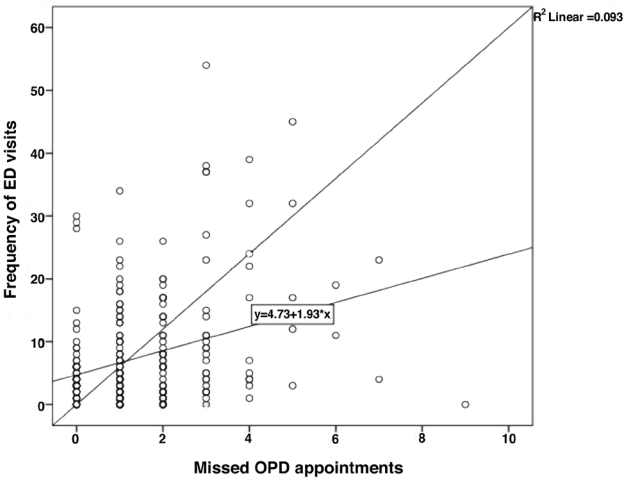

Figure 1 - Prediction of the frequency of expected emergency department (ED) visits through the missed appointment by the following linear regression equation: frequency of ED visits = 4.728+1.920× missed outpatient department (OPD) appointments for hematology clinic. R=0.31.

Table 3 - Independent sample t-test comparing mean of ED among different variables.

Variables	Number of ED visits	Mean	SD	Mean [CI]	*P*-value
Hydroxyurea					
On hydroxyurea	58	8.79	9.33	1.5 [-1.18,4.18]	0.270
Not on hydroxyurea	189	7.29	8.97		
Folic Acid					
On folic acid	192	8.14	9.60	2.21 [-0.51, 4.93]	0.530
Not on folic acid	55	5.93	6.63		
Comorbidities					
With comorbidities	55	14.91	11.79	9.35 [6.89, 11.81]	<0.001
Without comorbidities	192	5.56	6.84		

There's no significant difference in the mean of emergency department (ED) among the following variables: gender, and hydroxyurea, and folic acid prophylaxis. A significant difference is found comparing mean of ED visits in patients with and without comorbidities.

Discussion. This study aim to evaluate the relation between the frequency of ED visits and OPD visits in sickle cell pediatric patients. The correlation between OPD and ED visits was not statistically significant. This finding could be attributed to some existing variations in OPD and ED utilization among SCD patients such as gender, age, socioeconomic status, comorbidities,

family income, educational level, and accommodation distance to hospital. Oyenubi et al[18] studied factors that predict OPD utilization in SCD patients in the USA and found that age, other comorbidities, average family income had significantly influenced the use of OPD and ED in SCD patients. However, in our study we could not assess previous factors due to deficiency in the electronic system. In addition, the sample size was relatively moderate so statistical power could be low to detect a modest correlation.

However, there was a significant correlation between ED visits and missed hematology OPD appointments. In this study, from total OPD visits, there were 23% missed appointments, which can be caused by multiple factors related to parents' limitations, such as commitment to the daily job, traveling for long-distance to reach the hospital, other childcare, and lack of transportation. Also, parental anxiety during acute crises and the fear of consequences of delayed medical consultation may contribute to seeking for urgent care more frequently, such as emergency department care, and hence not attending OPD appointments.[19] Furthermore, a study found that children who visited the ED once a year were more likely to have 2 or more ED visits in the same year.[20]

Morey et al[17] conducted a study to assess age-related EDR in SCD patients and found that EDR was less than 0.15 in patients younger than 15 years of age and started to increase thereafter. However, the mean EDR in our study population was 0.43, which is higher than the previously explained cut-off value (0.33) and the study (0.15) result of Morey et al.[17]

Teresa et al[21] showed ED visits/patient/year was 0.39 for patients between 0-9 and 0.59 for patients between 10-18 years old. While in David et al[8] ED visits/patient/year were 0.63 (0-9 years old) and 0.7 (10-18 years old). However, ED visits/patient/year in our study was significantly higher: 2.93 (4-9 years old) and 2.27 (10-18 years old).

In this study, there was a significant increase in ED utilization among SCD patients with another comorbidity. However, there was no relationship between the number of OPD visits and having other comorbidity. While a previous study showed that SCD patients with comorbidity had higher OPD visits in relation to the patients without comorbidity.[18]

Regarding the frequency of ED visits, this study found no significant difference between patients who were on hydroxyurea and patients who were not on hydroxyurea. Similarly, a study done by Bejan et al.[22] showed no significant difference in the rate of painful crisis before and after hydroxyurea. Although, it was approved by food and drug administration (FDA) as hydroxyurea has proven clinical and laboratory effects on SCD patients as it decreases the occurrence of VOE, which is the most common presentation to the ED.[9,23,24] In addition, it improves the clinical outcome for the patient as it prevents sickle cell related injury to the kidney, spleen, and brain.[25] Previous studies showed that adherence to hydroxyurea decreases the rate of hospitalization, ED visits, and health care cost.[23,26]

This study also showed no significant difference between patients who were on folic acid and patients who were not on folic acid regarding the frequency of ED visits. Similarly, Rabb et al[27] conducted a clinical trial on patients with folic acid and found no difference between the folic acid and the placebo group regarding acute splenic sequestration, painful episodes, dactylitis episodes, minor or major infection, with even hemoglobin measurement. Another study also showed no difference in reticulocyte count or hemoglobin level after discontinuation of folic acid.[28]

One of the study's major limitations is inability to adjust estimates of correlation between ED visits and missed hematology OPD appointments, and it might be possible that the adjusted estimates of association are different from unadjusted associations. Another limitation was the shortage of medical system information in which the following types of data were not available: patient residency, number of SCD patients within a family, disease severity, parents' educational level, and whether the reason for the ED visit is related to sickle cell emergency or any other reason. However, the data is collected from the electronic system avoiding recall bias. Also, the type of data is purely objective to overcome subjectivity. Moreover, the study included all SCD patients who met the inclusion criteria during the study period.

A program is recommended to educate the patients and their parents on the importance of follow -up in the OPD. In order to improve compliance, further studies are needed for a better understanding of the factors contributing to OPD noncompliance.

In conclusion, SCD children in this study reported a high rate of ED visits. Although no significant correlation was detected between the frequency of ED visits and OPD visits in sickle cell pediatric patients, children with missed hematology OPD appointments had more ED visits. Thus, ED visits can be predicted from the frequency of missed OPD appointments. These findings suggest that regular OPD visits can improve management of the disease.

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