Original Article

Presentation of Acute Pancreatitis in Sickle Cell Disease Patients: A Single Hospital Experience

Saeed Al-Hindi, Zahra Khalaf[1], AbdelSalam N. Al-Sousi[1]

Department of Pediatric Surgery, Salmaniya Medical Complex, Manama, Kingdom of Bahrain, [1]Department of Postgraduate Surgical Studies, Royal College of Surgeons in Ireland, Dublin, Ireland

Abstract

Introduction: Sickle cell disease (SCD) is a haemoglobinopathy that leads to the formation of distorted sickle-shaped red blood cells that are prone to vaso-occlusion. This may lead to vaso-occlusive crises that may affect any organ. Acute pancreatitis (AP) in SCD patients may be mimicked by a vaso-occlusive crisis in the abdomen. The objective of this article is to analyse the clinical profiles of SCD patients with AP and understand the differences in the presentation of AP compared to an abdominal vaso-occlusive crisis and the difference between its presentation in SCD patients in comparison to other patients. **Materials and Methods:** Twenty-eight SCD patients who were diagnosed with AP during their admission to the paediatric department at a tertiary hospital between January 2012 and December 2020 were retrospectively studied. Patients aged older than 14 years were excluded. The data collected concerned: demographics, the clinical course and the hospital course. The diagnosis and severity protocols followed the revised Atlanta Criteria. **Results:** The patients were aged with a mean of 9.61 years. There were 15 males and 13 females. Demographics were not significantly correlated to complication rates ($P > 0.05$). The mean duration of hospitalisation was 6.43 days. The most common clinical presentations were abdominal pain, fever, then vomiting and nausea. Three patients experienced complications and they were all cases of cholangitis (10.71%). There were no cases of pseudocysts, acute necrotic collections, pancreatic or peripancreatic necrosis or walled-off necroses. All of the cases of AP in SCD children were mild according to the revised Atlanta classification. Leucocytosis was present in 29.29% of patients and 17.8% of patients had high C-reactive proteins (CRPs). There was no significant correlation between leucocyte counts, CRP levels, serum or urinary amylase levels and complications ($P > 0.05$). All patients had haemoglobin (Hb) levels above 7 g/dL. The levels of sickle Hb ranged from 40 to 70 g/dL and reticulocyte counts averaged at 3.57%. Haematologic parameters were not significantly correlated with complication rates ($P > 0.05$). There were no recurrences. **Conclusion:** AP in SCD patients presented with classic signs and symptoms. There were no associations between demographics and complications. The levels of leucocytes, CRP counts and serum and urinary amylase were not correlated with complications. The level of Hb and sickle cell Hb was not associated with complication rates. Reticulocytes were slightly elevated in SCD patients with AP. More studies are needed to demarcate factors distinguishing AP in SCD from abdominal vaso-occlusive crises.

Keywords: Acute pancreatitis, clinical profile, sickle cell disease, vaso-occlusive

Introduction

Sickle cell disease (SCD) is an autosomal recessive inherited haemoglobinopathy. It is attributed to a homozygous sickle beta-globin gene mutation that forms sickle haemoglobin (Hb), a heterozygous mutation that combines sickle Hb with Hb C or beta-thalassemia mutations. This leads to the formation of rigid, distorted sickle-shaped red blood cells with pronation to cause vaso-occlusion. This results in painful crises that may affect a range of organs and more serious complications.[1] The Centres for Disease Control and Prevention have estimated that about 100,000 Americans are affected by SCD, with a higher pre-dominance amongst African Americans (1 out of every 365 African Americans).[2]

Acute painful crises (vaso-occlusive crises) commonly occur in SCD patients and often require hospitalisation. Vaso-occlusive crises usually begin by the age of 6 and they manifest as pain

Received: 07-10-2022 **Revised:** 03-01-2023 **Accepted:** 16-01-2023 **Available Online:** 10-04-2023

Access this article online

Quick Response Code:

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

DOI: 10.4103/ajps.ajps_133_22

Address for correspondence: Dr. Zahra Khalaf, Department of Postgraduate Surgical Studies, Royal College of Surgeons in Ireland, Dublin, Ireland.
E-mail: zahra.khalaf@hotmail.com

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Al-Hindi S, Khalaf Z, Al-Sousi AN. Presentation of acute pancreatitis in sickle cell disease patients: A single hospital experience. Afr J Paediatr Surg 2024;21:151-4.

in any part of the body, including the extremities, back, chest and abdomen. They may additionally be accompanied by a fever. A patient of known SCD history presenting with the aforementioned symptoms must undergo multiple routine laboratory examinations including a full blood count with differentials, a liver function test and inflammatory markers because the actual cause could be another detrimental condition that is misattributed to the pain of sickle cell origin.[3]

A crucial differential of a vaso-occlusive crisis in the abdomen in SCD patients is acute pancreatitis (AP). Biliary causes are the most common cause of AP in children.[4] Other causes of paediatric AP are infections, trauma, toxicity, anatomical, systemic diseases and idiopathic.[5] AP notoriously presents as severe epigastric pain, mimicking a sickle cell crisis, which is why this differential may be neglected in a patient with a known history of SCD. It is of paramount importance to recognise AP in a patient with SCD to appropriately treat the patient and prevent further morbidity or even mortality in extreme cases.[6,7] The objective of this article is to analyse the clinical profiles of SCD patients with AP with the ultimate goal of helping clinicians suspect AP as opposed to a vaso-occlusive crisis in patients with SCD.

Materials and Methods

Inclusion and exclusion criteria

The clinical profiles of paediatric SCD patients who were diagnosed with AP were studied in a retrospective manner. A total of 28 patients were included. The inclusion criteria were as follows: All SCD inpatients who were diagnosed with AP during their admission to the Paediatric Department at a single tertiary hospital, Salmaniya Medical Complex, between January 2012 and December 2020. The exclusion criterium was patients aged more than 14 years old; the rationale for this cutoff age is the Paediatric Department's age limits within the hospital the study was set in.

Data collection

Patients' medical records were searched for patients' clinical assessments, hospital courses and investigations. The data collected encompassed patient demographics, clinical manifestations (signs and symptoms), investigations, hospital course and outcomes. The laboratory investigations included white blood count (WBC), C-reactive protein (CRP), serum amylase, urinary amylase, Hb levels (grams per decilitre [g/dL]), sickle haemoglobin (HbS) and reticulocyte count. Meanwhile, the radiological investigations included ultrasounds, computed tomography (CT) and magnetic resonance imaging (MRI). Patients' hospital course was assessed in terms of the duration of hospitalisation, duration of intensive care unit (ICU) admission, complication rates and types and feeding status. Moreover, the patients' follow-up durations were also recorded.

Diagnosis and severity classification protocols

The Atlanta criteria were used to diagnose AP. The criteria outline the following: (1) The presence of abdominal pain concordant with the presentation of pancreatitis (pain situated in the epigastric region which may radiate to the back), (2) Elevations in amylase or lipase by at least a factor of three and (3) Radiological findings characteristic of AP (on ultrasound, CT or MRI). In order for a diagnosis to be made, at least two of the predefined criteria had to be present.

The severity of AP was also classified using the revised Atlanta classification. Cases were considered mild in the absence of organ failure and complications (whether local or systemic), moderate if there was organ failure that resolved within <48 h and severe in cases of persistent organ failure beyond 48 h.[8]

According to hospital protocol, SCD patients with SCD were admitted to the ICU as a routine measure due to the tendencies SCD patients to deteriorate quickly. Therefore, the ICU admissions were not attributed to the clinical severity of patients' conditions. However, the length of ICU stay was individualised to patients' clinical needs and speed of recovery.

Statistical analysis

We used SPSS statistics software, version 27 (IBM Corp, Chicago, IL, USA) to statistically analyse the data. We used frequencies, means and ranges to depict continuous and categorical variables. The categorical variables were further examined using Chi-squares. The significance of correlations between variables was assessed using *P* values; *P* values were considered significant if they were 0.05 or less.

Ethical considerations

This study was granted ethical approval by the responsible committee, the Ministry of Health Research Committee.

Results

A total of 28 paediatric patients with SCD presented to a Salmaniya Medical Complex within the pre-defined timeframe and were eligible for inclusion. The patients were aged a mean of 9.61 years, with ages ranging from 7 to 14 years of age. There was no correlation between gender and complication rates ($P = 0.65$) or the patients' mean ICU stays [$P = 0.89$, Table 1].

The duration of hospitalisation ranged from 4 to 16 days (mean: 6.43 days). Meanwhile, all of the SCD paediatric patients were

Table 1: Patient demographics in relation to the frequency of complications and intensive care unit stay

	Frequency, *n* (%)	Complications, *n* (%)	Mean ICU stay in days (range)
Gender (*P*)		0.65	0.89
Males	15 (50)	2 (13.33)	4.47 (3-8)
Females	13 (43.3)	1 (7.69)	4.38 (3-8)
Age (years) (*P*)		0.94	0.95
≤7	2 (7.14)	0	4 (3-5)
8-14	26 (92.86)	3 (11.5)	4.46 (3-8)

ICU: Intensive care unit

Table 2: The clinical presentation of paediatric acute pancreatitis

Clinical symptom or sign	Frequency, *n* (%)
Abdominal pain	28 (100)
Fever	17 (60.7)
Vomiting	15 (53.6)
Nausea	5 (17.9)

Table 3: Laboratory parameters in relation to complications and duration of intensive care unit stay

Parameter	Frequency, *n* (%)	Complications (%)	ICU stay (mean days)
Leucocyte count (cumm) (*P*)		0.56	0.64
≤11,000	17 (60.71)	3 (17.65)	4.71
>11,000	11 (29.29)	0	4
CRP (mg/dL) (*P*)		0.95	0.42
≤5	23 (82.14)	3 (13.04)	4.57
>5	5 (17.86)	0	3.8
Serum amylase (U/L) (*P*)		0.36	0.14
≤110	4 (14.29)	1 (25)	5.75
>110-≤500	9 (32.14)	0	4.22
>500-≤1000	14 (50)	2 (14.3)	4.14
>1000	1 (3.57)	0	5
Urinary amylase (U/L) (*P*)		0.54	0.084
≤500	2 (7.14)	1 (50)	6
>500-≤1000	15 (53.57)	1 (6.7)	4.2
>1000	11 (39.29)	1 (9.1)	4.45

ICU: Intensive care unit, CRP: C-reactive protein

Table 4: Haematologic parameters in relation to complications and duration of intensive care unit stay

Parameter	Mean (range)	*P*-values in relation to complications (%) (*P*)	*P*-values in relation to ICU stay (*P*)
Hb (g/dL)	8.4 (7.5-9)	0.87	0.93
HbS (g/dL)	53.39 (40-70)	0.31	0.19
Reticulocyte count (%)	3.57 (2-5)	0.52	0.42

Hb: Haemoglobin, HbS: sickle haemoglobin

routinely admitted to the ICU due to the tendency of SCD to deteriorate quickly, not due to the severity of the condition. The duration of ICU stay ranged from 3 to 8 days (mean: 4.43 days).

The most common clinical symptoms were abdominal pain, then vomiting and nausea. Seventeen patients also experienced a concurrent fever (60.7%) [Table 2]. Patients routinely had ultrasound imaging and CT scans were done as indicated by their clinical conditions. A total of three patients experienced complications and they were all cases of cholangitis (10.71%). There were no cases of pseudocysts, acute necrotic collections, pancreatic or peripancreatic necrosis or walled-off necroses. All of the cases of AP in SCD children in this study were considered mild according to the revised Atlanta classification.[8]

The biochemical parameters were examined. Overall, 29.29% of the patients experienced leucocytosis and 17.8% of patients had elevated CRP levels. Mostly, both serum and urinary amylase levels ranged between >500 and ≤1000 U/L as it accounted for 50% and 53.57% of the cases, respectively. There was no significant correlation between WBCs, CRP levels, serum amylase, or urinary amylase and complication rates or the duration of the children's ICU stay [$P > 0.05$, Table 3].

Regarding haematologic parameters, all patients had Hb levels above 7 g/dL. The levels of sickle Hb ranged from 40 to 70 g/dL and reticulocyte counts averaged at 3.57%. All of the aforementioned haematologic parameters were not significantly associated with the occurrence of complications or the duration of patients' ICU stay [Table 4].

The patients were followed up for a mean of 42.61 months. There were no cases of recurrences.

Discussion

AP is seldom included as a differential of abdominal pain in SCD patients.[9] There is a paucity in literature studying the presentation of AP in SCD patients. Hence, there is a need for more research on the topic to allow a better assessment of AP's incidence and presentation in the SCD population. Understanding the presentation of AP in SCD patients may assist clinicians in diagnosing it early as well as distinguishing it from abdominal vaso-occlusive crises to ultimately improve patient care.[10]

In this particular study, we have combined and analysed retrospective data from a cohort of 28 SCD patients who were diagnosed with AP in a single tertiary centre. In this subset of patients, no significant association was found between gender and complication rates ($P = 0.65$) or mean ICU stay ($P = 0.89$). All of the patients (100%) presented with abdominal pain, 60.7% had a concurrent fever, 53.6% had concurrent vomiting and only 5 (17.9%) of the patients had nausea. These results are comparable to the clinical manifestations of vaso-occlusive crises as described by Gardner and Jaffe and Akingbola *et al*., whereby the most commonly associated symptoms were vomiting (60%) and bone pains (45%), yet the latter did not occur in any of our patients.[11,12] Fever is another clinical parameter that is often found in vaso-occlusive disease, yet it is commonly low grade, therefore, a body temperature of 38°C and higher warrants further investigations to rule out other causes.[3]

The rise in certain biochemistry parameters was considerably variable. Leucocytosis was found in 29.29% of the patients, with elevated CRP in 17.8%. Elevated CRP and leucocytosis are non-specific variables and are additionally seen in vaso-occlusive crisis patients which is a common cause of abdominal pain encountered by most SCD patients.[13,14] The

elevated serum and urine amylase levels in the vast majority of the patients are expected and are consistent with the findings of AP in non-SCD patients.[15] However, the level of elevations of serum and urinary amylase was not significantly correlated with complication rates, and $P = 0.36$ and 0.54, respectively.

With regard to haematological parameters, including Hb levels (Hb), sickle Hb levels (HbS) and reticulocyte count (%), there was also no link to the length of ICU stay or complication rates ($P \geq 0.05$). When comparing the haematological parameters to those seen in vaso-occlusive crises, a study conducted by Lopez *et al*. showed a mean Hb value of 8.4 g/dl in patients admitted for a vaso-occlusive event, which is equivalent to the mean value of Hb seen in our patients, yet the mean reticulocyte count of 9.2% was higher than that seen in our study (3.57%).[16]

A number of limitations can be identified in this study. Due to the retrospective nature of the study, the variables studied were limited. A number of other factors could have been explored such as lactate dehydrogenase levels, bilirubin levels and the grade of the fever at presentation. Furthermore, the small cohort of patients included may have limited the deduction of significant correlations. Moreover, there was a lack of data to compare the results to as the presentation of AP in SCD patients is an under-researched field. More studies should be conducted to allow for more studies that assess the presentation of AP in SCD as opposed to abdominal vaso-occlusive crises and other abdominal differentials.

Conclusion

AP is a differential diagnosis that may be missed in SCD patients presenting with acute abdominal pain. This subset of patients should be carefully assessed and sufficient laboratory testing should be carried out before finalising a diagnosis of the similarly presenting vaso-occlusive crisis. Accurate and early diagnosis of AP in an SCD patient avoids unnecessary treatment and delayed appropriate treatment. Our study mainly found that the presentation of AP in SCD patients was similar to the presentation of AP in those who do not have SCD. AP in SCD was found to be mild and self-limiting in our cohort. There was no correlation between demographical data such as gender or age and length of ICU stay or complication rate. There was no association between biochemical and haematological values with complication rates or length of ICU stay. However, as anticipated reticulocyte counts were less in AP in comparison to those seen in vaso-occlusive crises. The studies addressing this topic are scarce and there is a need for more well-designed studies studying the clinical profiles of AP in SCD patients to clearly demarcate factors distinguishing AP in SCD from abdominal vaso-occlusive crises and aid in deriving an early diagnosis and more optimal outcomes.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Steinberg MH. Mechanisms of vasoocclusion in sickle cell disease. 2016. www.uptodate.com.
2. National Center on Birth Defects and Developmental Disabilities CfDCaP. Data & Statistics on Sickle Cell Disease. Available from: https://www.cdc.gov/ncbddd/sicklecell/data.html. [Last updated on 2022 May 02].
3. Borhade MB, Kondamudi NP. Sickle cell crisis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022.
4. Vichinsky EP, Haberkern CM, Neumayr L, Earles AN, Black D, Koshy M, *et al*. A comparison of conservative and aggressive transfusion regimens in the perioperative management of sickle cell disease. The preoperative transfusion in sickle cell disease study group. N Engl J Med 1995;333:206-13.
5. Suzuki M, Sai JK, Shimizu T. Acute pancreatitis in children and adolescents. World J Gastrointest Pathophysiol 2014;5:416-26.
6. Gapp J, Chandra S. Acute pancreatitis. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482468/. [Last updated on 2022 Jun 21].
7. Jasti S, Williams V, Vamadevan A, Gillette P, Gress F. Prevalance of acute pancreatitis in sickle cell disease: 236. J Am Coll Gastroenterol ACG 2008;103:S91-S2.
8. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, *et al*. Classification of acute pancreatitis – 2012: Revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102-11.
9. Ahmed S, Siddiqui AK, Siddiqui RK, Kimpo M, Russo L, Mattana J. Acute pancreatitis during sickle cell vaso-occlusive painful crisis. Am J Hematol 2003;73:190-3.
10. Kumar DM, Choppari K, Thomas SRJ.Acute pancreatitis in a child with sickle cell anemia. Int J Contemp Pediatr 2020;7:1174-6.
11. Gardner CS, Jaffe TA. CT of gastrointestinal vasoocclusive crisis complicating sickle cell disease. AJR Am J Roentgenol 2015;204:994-9.
12. Akingbola TS, Kolude B, Aneni EC, Raji AA, Iwara KU, Aken'Ova YA, *et al*. Abdominal pain in adult sickle cell disease patients: A Nigerian experience. Ann IB Postgrad Med 2011;9:100-4.
13. Okocha C, Manafa P, Ozomba J, Ulasi T, Chukwuma G, Aneke J. C-reactive protein and disease outcome in Nigerian sickle cell disease patients. Ann Med Health Sci Res 2014;4:701-5.
14. Oluwagbenga OO, Ndububa DA, Musah Y, Bolarinwa RA, Ayoola OO. Clinical and biochemical manifestations of severe sickle cell anemia in adult patients in steady state in Ile-Ife, Nigeria. Sudan J Med Sci 2019;14:52-63.
15. Wani MD, Chalkoo M, Ahmed Z, Yousuf AM, Arafat Y, Arsalan SS, *et al*. Clinical significance of urinary amylase in acute pancreatitis. Arch Surg Clin Res 2017;1:021-31.
16. Lopez BL, Griswold SK, Navek A, Urbanski L. The complete blood count and reticulocyte count – Are they necessary in the evaluation of acute vasoocclusive sickle-cell crisis? Acad Emerg Med 1996;3:751-7.