South Thames Sickle Cell & Thalassaemia Network

# STSTN Guidelines for the Diagnosis and Management of Acute Chest Syndrome in Adult Sickle Cell Disease Patients

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These guidelines have been updated and are based on the 2015 BCSH guidelines on management of Acute Chest Syndrome in sickle cell disease

Acute chest syndrome (ACS) is a serious and potentially life threatening complication of sickle cell disease is defined as an acute illness characterised by fever and/or respiratory symptoms, accompanied by a new pulmonary infiltrate on chest X-ray (Charache et al, 1979; Ballas et al, 2010). The clinical progression of ACS can be rapid, leading to respiratory failure. Vigilance throughout admission for the development of this complication is essential. Early recognition and prompt intervention usually results in clinical improvement. Conversely, delay in recognition and treatment can lead to adverse outcomes. ACS occurs in all genotypes of sickle cell disease (SCD).

**Pathophysiology of Acute chest syndrome**

The aetiology of acute chest syndrome is multifactorial, the initial insult may be infection, fat embolism from infarcted bone marrow and/or intravascular pulmonary sequestration of sickle cells, leading to lung injury and infarction. This results in a vicious cycle of hypoxia, HbS polymerisation, vaso-occlusion and altered pulmonary flow.

Infections with either bacterial or viral pathogens are implicated more commonly in children than adults. A pre-existing diagnosis of asthma has also been shown to be associated with an increased incidence of ACS in children.

Severe bony pain from rib infarcts may cause splinting leading to regional hypoventilation, and opiate narcosis e.g. following a general anaesthetic. This can result in alveolar hypoventilation and an ACS.

**Clinical features**

The clinical features of ACS may not be evident at the time of admission. Consider prodromal phase ACS in all patients admitted with a painful crisis.. Nearly half of patients present with a painful vaso-occlusive crisis and then develop this complication whilst in hospital. ACS often develops 24–72 h after the onset of severe pain (Gladwin &

Vichinsky, 2008). ACS may develop post-operatively, especially following abdominal surgery, and in patients not receiving a pre-operative blood transfusion (Howard et al,2013).

The most common respiratory symptoms of ACS are:

- Cough
- Chest pain (which may be pleuritic) and
- Shortness of breath

Other features may also be present:

- Wheeze
- Fever
- Hypoxia
- Tachypnoea
- Tachycardia
- Skeletal pain
- Haemoptysis

Chest signs include crepitation's, bronchial breath sounds, reduced air entry and dullness to percussion. Rhonchi and pleural rubs may be heard, and in children intercostal recession, nasal flaring and other signs of increased work of breathing may be seen. Clinical signs often precede chest X-ray findings, but chest examination may be normal in the early stages. Close monitoring should be undertaken where there is clinical suspicion.

**Diagnosing ACS**:

Acute chest syndrome is defined as the presence of a new pulmonary infiltrate on chest X-ray in combination with respiratory symptoms and/or fever in a patient with sickle cell disease. It is largely a clinical diagnosis, particularly in the initial stages, and diagnosis is straightforward when with the usual clinical features present to an experienced clinician. The diagnosis can be difficult to make when there is a lag between radiological features, and in cases with less clear clinical features. The clinical features of ACS overlap with the clinical features of pneumonia, and ACS is often precipitated by infection. However, treating ACS as a purely infective episode may lead to progression and rapid clinical deterioration.

- A chest X-ray is required in any patient with hypoxia, chest pain, respiratory symptoms or fever ***but*** must not delay the institution of urgent clinical

management if the patient is very unwell or has rapidly progressive respiratory deterioration

- The chest X-ray may be normal initially, even in the presence of significant respiratory distress.

- Any patient with oxygen saturation < 94% or a fall 3% or more from baseline needs to be reviewed by medical staff immediately and appropriate action taken.

- Close monitoring should be instituted together with supportive measures, which may include urgent transfusion, particularly in the presence of severe hypoxia.

- Although patients may have characteristic clinical features on initial presentation, 50% of patients with acute chest syndrome present initially with a painful crisis before developing ACS. Vigilance is essential in patients admitted with vaso-occlusive crisis and especially in patients recovering post-surgery, particularly following abdominal surgery.

- Adequate monitoring on the ward is essential to prevent morbidity and mortality from this condition.

  Ensure at least four hourly pulse oximetry and respiratory rate, and Daily chest examination.

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**Differential diagnosis of hypoxia in sickle cell disease**

1. Chest infection

Clinically, ACS may be indistinguishable from a purely infective episode. If in doubt, treat for both. All patients with ACS should receive intravenous antibiotics as part of their management.

2. Pulmonary embolism

Typically presents with pleuritic chest pain, hypoxia and a normal chest X-ray, D-dimers are not helpful in SCD, as they tend to be elevated. On clinical suspicion, diagnostic imaging with Ventilation perfusion scan (VQ scan), CT Spect OR CT pulmonary angiogram
(CTPA) should be performed and treatment dose low molecular weight heparin initiated pending CT report. ACS may be complicated by pulmonary embolism or may occur secondary to pulmonary embolism. In such cases, treatment will be required for both conditions simultaneously.

3. Over-narcosis (Opiate toxicity)
Careful monitoring should avoid this untoward effect of opiates. Regular monitoring of respiratory rate, sedation and pain scores should be in place. Opiate narcosis is associated with a falling respiratory rate. Opiate dose modification or discontinuation may be necessary. Naloxone may be required to reverse significant opiate toxicity. Opiate narcosis may trigger or worsen ACS.

4. Hypoventilation due to pain
Effective analgesia is necessary to prevent hypoxia and hypercapnia developing due to a restrictive ventilatory defect as a consequence of ongoing chest pain. This may contribute to the development of ACS.

5. Fluid overload
Fluid replacement is an integral part of the management of ACS. However, overhydration may lead to pulmonary vascular congestion and pulmonary oedema, especially in patients with decreased cardiac function. Close attention should be paid to fluid balance and a fluid balance chart must be maintained. Acute deterioration in a patient after blood transfusion should prompt consideration of fluid overload or transfusion-related acute lung injury (TRALI)

**Investigations**

- Chest X-ray
- Full blood count
- Biochemistry (Creatinine and LDH)
- Arterial blood gases on adults
    - If SpO2 < 94% on air
    - On room air if clinically safe (i.e. not in respiratory distress and SpO2 >85% when off Oxygen)
- Group and antibody screen (Cross match blood as necessary)
- Microbiology
    - Sputum for microscopy,culture and sensitivity
    - Nose and throat swab for respiratory viruses in patients with coryzal symptoms
    - Consider urine for pneumococcal and Legionella antigen
    - Consider nasopharyngeal aspirate for chain reaction (PCR) for viruses

**Management**
The immediate aim of treatment in ACS is to prevent or reverse acute respiratory failure.

- Involve Consultant Haematologist/Haematology SpR as soon as ACS is suspected

- Liaise with high dependency /intensive care unit even in mild cases, as clinical deterioration is often rapid and unexpected. Early warning track and trigger systems should be in place.

In low prevalence areas consider HDU management from outset and transfer to a specialist sickle centre.

- Vital signs including sedation scores will need to be assessed at least 4 hourly or more frequently depending on the patient's clinical condition. Continuous pulse oximetry is desirable when there is clinical concern.

- Clinical review at least four hourly.

- Pain control

Adequate analgesia in patients with rib, thoracic or abdominal pain is recommended so as to prevent splinting of the diaphragm and the consequent vicious cycle of hypoventilation, atelectasis, hypoxia and sickling that can occur.
Effective pain relief, using the World Health Organization analgesic ladder is an important aspect of the management of ACS. Monitor to prevent alveolar hypoventilation due to opioid excess . Non-steroidal anti-inflammatory drugs are useful.

- Transfusion

Not all patients with ACS will require a blood transfusion and the decision to transfuse may be difficult. A senior decision maker should be involved.
While there are no randomised controlled trials, there is observational and case control evidence for the efficacy of transfusion in ACS and it can be lifesaving in severe cases. The degree of hypoxia and respiratory compromise partly governs the need for and mode of blood transfusion. Prompt transfusion often results in a fairly rapid response as rapid reduction in HbS and improvement in overall haemoglobin is more important than a specific target haemoglobin S%.
Simple top up transfusion may suffice early in the course of ACS and may also be used if Hb is <70g/l, aiming for a post transfusion haemoglobin no greater than 100g/l. When indicated, exchange transfusion should be carried out, manually if automated red cell exchange is not readily available. Exchange transfusion is indicated in the following circumstances:

- PaO2 < 9kPa on air
- Deteriorating patient
- Respiratory distress
- Multi-lobe lung infiltrates

- When a top up transfusion is likely to result in a detrimental increase in blood viscosity (i.e. haemoglobin is > 90 g/L)
- In the presence of other significant acute organ dysfunction
- Progression or limited improvement following top up transfusion.

Exchange blood transfusion in this setting, should ideally be carried out on a monitored unit such as HDU.
Blood for exchange transfusion should be sickle negative, preferably less than 7 days old and also matched for Rh D, C, E, c, e as well as Kell antigens, and antigen-negative for previous red cell antibodies.

- Oxygen therapy

Maintain SpO2 ≥ 95% or within 3% of the patient's baseline.

- Chest physiotherapy and Incentive spirometry.

Coupled with effective pain relief, incentive spirometry has been shown to be beneficial in children and young adults by reducing chest splinting and is likely to be a useful adjunct to other forms of therapy. The Sickle adult standard recommends it for all patients at risk of ACS
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- Advanced respiratory support

A minority of patients will require more intensive respiratory support. Worsening hypoxia, severe dyspnoea and increasing hypercapnia causing a respiratory acidosis (arterial pH <7.35) are indications for initiating advanced respiratory supportive therapies in a critical care environment.

- Antimicrobials

It is prudent to treat all patients empirically for severe community acquired pneumonia unless there are clinical data to suggest an alternative infection. Choice of antimicrobial will be guided by local policy. Close liaison with microbiology is helpful. Specific guidance is required for pandemic flu.

- Hydration

Intravenous crystalloid infusion should be given until the patient is able to drink adequate amounts of fluid. A fluid balance chart should be maintained and care taken to avoid fluid overload.

- Thromboprophylaxis is recommended for adults without contraindications

- Nebulised bronchodilators

Bronchodilators are beneficial, particularly in the presence of reactive airway signs or a history of asthma.

- Daily blood counts, urea and electrolytes and liver function tests should be performed until a trend towards normalization of abnormal values is observed.

- Others:

There is insufficient evidence to recommend its routine use of Nitric oxide.
There is insufficient evidence to recommend its routine use of Corticosteriods.

**Prevention**
Patients who present in sickle crisis with chest, sternal, rib or back pain, and post abdominal surgery patients, should commence incentive spirometry and or chest physiotherapy.

**Secondary prevention**
Hydroxycarbamide has been shown to reduce the incidence of ACS and should be considered in any patient who has one or more episode of acute chest syndrome. Physicians in low prevalence areas should consider referral to their local specialist centre for advice on initiation of hydroxycarbamide. Shared care using a common protocol may be appropriate. Hydroxcarbamide therapy should be monitored by FBC, retics and HbF according to an available protocol.

**Blood transfusion**
This should be considered prior to surgery in patients deemed to be particularly at risk. Factors such as past history of ACS, severity of sickle phenotype and type of planned surgery should be taken into account.

Other useful measures

- Optimize vaccination status (Meningococcal, Pneumococcal and Influenza vaccines)
- Penicillin prophylaxis (erythromycin if allergic to penicillin)
- Smoking cessation
- Consider echocardiogram including TRV max and pulmonary function tests – at least 4 weeks following the acute episode

***Criteria for transfer to the specialist centre from a local trust***

**Adults:** Discuss and consider for transfer adult patients presenting with ACS if:

a. uncertainty regarding management
b. unable to receive blood (religious or clinical reasons)
c. deteriorating despite early top up if no facilities for automated EBT locally
d. (ITU/HDU transfer)
e. developing multi-organ failure (ITU – ITU transfer advised)

**Contacts at specialist centres within the STSTN network :**

GSTT

Consultant Haematologist:
Jo Howard / Rachel Kesse-Adu
Telephone: 02071882741
Out of hours – Haematology SpR or on call consultant via switchboard (02071887188)

Clinical Nurse Specialists:
Neil Westerdale/Luhanga Musumadi / Tolu Adeosin
Telephone – 020 7188 7188 (switchboard) then bleep 1843

Kings College

Consultant Haematologist:
Moji Awogbade / Sara Stuart-Smith
Telephone: 02032999000
Out of hours – Haematology SpR or on call consultant via switchboard (020 32999 000)

Clinical Nurse Specialists:
Giselle Padmore-Payne and Fester Ike
Telephone – 020 3299 4968

St George's Hospital [AT to send details]

Consultant Haematologist:
Elizabeth Rhodes
Telephone: 020 87250885
Out of hours Haematology SpR via Switchboard 0208 6721255

Clinical Nurse Specialists:

Telephone – Switchboard 0208 6721255

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**For more info: The telephone numbers below are available Monday-Friday, 9am-5pm. Outside these hours, please contact your GP or go to your local Emergency Department (A&E).**

Guy's and St Thomas' Hospital Consultant Haematologist: Jo Howard / Rachel Kesse-Adu Telephone: 02071882741 Out of hours – Haematology SpR or on call consultant via switchboard (02071887188)

Evelina London Children's Hospital, Baba Inusa / Maria Pelidis 02071889432 or out of hours Haematology SpR via Switchboard (02071887188)

Kings College Hospital Consultant Haematologist: Moji Awogbade / Sara Stuart-Smith Telephone: 02032999000 Out of hours – Haematology SpR or on call consultant via switchboard (020 32999 000)

King's College Hospital Paediatric Haematology – Consultant of the week via switchboard 020 3299 9000 Sue Height/ David Rees/ Subarna Chakravorty, Out of hours: Haematology SpR on call via switchboard 020 3299 9000

St George's Hospital Consultant Haematologist: Alison Thomas, Elizabeth Rhodes and Julia Sikorska Telephone: 020 87250885 Out of hours Haematology SpR via Switchboard 0208 6721255

Additional contacts can be found on the STSTN website (www.ststn.co.uk)

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