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| **About the Measure** | |
| **Domain:** | Sickle Cell Disease Pregnancy |
| **Measure:** | Acute Chest Syndrome |
| **Definition:** | Acute chest syndrome is a heterogenous complication of sickle cell disease caused by blockage of lung blood vessels by sickled red cells and characterized by fever, hypoxia, leukocytosis, and new pulmonary infiltrates. |
| **Purpose:** | Acute chest syndrome (ACS) occurs in both children and adults with sickle cell disease (SCD). ACS is a life-threatening emergency in SCD contributing to morbidity, hospitalization, and death. |
| **Essential PhenX Measures:** | Chest X-ray (810201) |
| **Related PhenX Measures:** | NA |
| **Measure Release Date:** | Toolkit Team to add |

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| **About the Protocol** | |
| **Protocol Release Date:** | Toolkit Team to add |
| **PhenX Protocol Name:** | Acute Chest Syndrome - General Populations |
| **Keywords:** | Pneumonia, respiratory complications, respiratory infection, lung congestion, sickle cell disease complications, SCD, acute chest syndrome, ACS. |
| **Protocol Name from Source:** | Cure Sickle Cell Initiative (CureSCi) Form 4e\_F2910 Acute Chest Syndrome |
| **Description:** | Items in this protocol, which are obtained via medical record abstraction, include acute chest syndrome (ACS) symptoms, results of vitals, physical examination, laboratory tests, and imaging procedures, whether transfusion was required, and severity of ACS. The form also includes a module for Rapid Progression to Acute Chest Syndrome. |
| **Specific Instructions:** | The Sickle Cell Disease Pregnancy Working Group (WG) recommends that investigators review the original case report form (CRF) from the Cure Sickle Cell Initiative (<https://curesickle.org/>) for additional context and instructions. The data elements below with an asterisk are “Core” for the Cure Sickle Cell Initiative.  The WG recommends that investigators review [Acute Chest Syndrome – Pregnancy](https://www.phenxtoolkit.org/protocols/view/890601) in the PhenX Toolkit.  The items under “Imaging” include a response about whether the imaging was not done due to pregnancy. The WG notes that required imaging is not harmful to the fetus and should not be withheld from the mother by virtue of pregnancy. The WG recommends removing this option when it is administered, and we can then indicate with an asterisk that this was in the original protocol but is no longer felt relevant with current standard-of-care practices. |
| **Protocol:** | **Acute Chest Syndrome During Pregnancy With Sickle Cell Disease**  **\*Acute Chest Syndrome**  [ ] Yes  [ ] No  [ ] Unknown  **If yes, indicate the following:**  Symptoms  1. Pleuritic Chest Pain  [ ] Yes  [ ] No  [ ] Unknown  2. Chest pain  [ ] Yes  [ ] No  [ ] Unknown  3. Wheezing  [ ] Yes  [ ] No  [ ] Unknown  4. Cough  [ ] Yes  [ ] No  [ ] Unknown  5. Dyspnea  [ ] Yes  [ ] No  [ ] Unknown  Vitals  1. \*Temperature (highest on day of diagnosis) \_\_\_\_\_\_\_\_\_\_\_\_\_\_  2. \*Heart rate (highest on day of diagnosis) \_\_\_\_\_\_\_\_\_\_\_\_\_\_  3. \*Respiratory rate \_\_\_\_\_\_\_\_\_\_\_\_\_\_  4.\*Systolic blood pressure on day of diagnosis \_\_\_\_\_\_\_\_\_\_\_\_\_\_  5.\*\*SpO2 (O2 saturation) in room air (FiO2 = 0.21) decreased by 2% or more from baseline \_\_\_\_\_\_\_\_\_\_\_\_\_\_  6. Oximetry  [ ] Yes  [ ] No  [ ] Unknown  a.\*O2 Saturation Value: \_\_\_\_\_\_\_\_\_\_\_\_\_\_  7. \*PaO2 < 60 mmHg  [ ] Yes  [ ] No  [ ] Unknown   1. \*PaO2 Value: \_\_\_\_\_\_\_\_\_\_\_\_\_\_     Physical Exam  1. Rales on lung auscultation  [ ] Yes  [ ] No  [ ] Unknown  2. Intercostal retractions  [ ] Yes  [ ] No  [ ] Unknown  3. Nasal flaring or use of accessory muscles of respiration  [ ] Yes  [ ] No  [ ] Unknown  4. Wheezing  [ ] Yes  [ ] No  [ ] Unknown  Diagnostic  Laboratory  1. Leukocytosis  [ ] Yes  [ ] No  [ ] Unknown  2. Decreased hemoglobin  [ ] Yes  [ ] No  [ ] Unknown  3. Decreased platelet count  [ ] Yes  [ ] No  [ ] Unknown  Imaging  1. Development of new infiltrate on chest x-ray and/or perfusion defect demonstrable on lung radioisotope scan  [ ] Yes  [ ] No  [ ] Unknown  [ ] Unable to perform due to pregnancy (*this question may not be applicable now but in previous definitions*)  2. A new pulmonary infiltrate involving at least one complete lung segment that is consistent with the presence of alveolar consolidation, but excluding atelectasis  [ ] Yes  [ ] No  [ ] Unknown  [ ] Unable to perform due to pregnancy  3. Pulmonary infiltrate  [ ] Yes  [ ] No  [ ] Unknown  [ ] Unable to perform due to pregnancy  4. Radiographic evidence of consolidation. A new segmental (involving at least one complete segment) radiographic pulmonary infiltrate  [ ] Yes  [ ] No  [ ] Unknown  [ ] Unable to perform due to pregnancy    Therapy  1. Transfusion  [ ] Yes  [ ] No  [ ] Unknown  a. If yes, type  [ ] Simple  [ ] Exchange  Severity  1. Admitted to Hospital  [ ] Yes  [ ] No  [ ] Unknown  2. ICU  [ ] Yes  [ ] No  [ ] Unknown  3. Mechanical Ventilation  [ ] Yes  [ ] No  [ ] Unknown  a. The length of time received mechanical ventilation  4. Respiratory support  Non-mechanical ventilatory support:  [ ] Simple nasal cannula  [ ] Face mask O2 (e.g., venti mask, non-rebreather)  Noninvasive mechanical ventilatory support:  [ ] CPAP  [ ] SiPAP  [ ] BiPAP  [ ] High flow nasal cannula (HFNC)  Invasive mechanical ventilatory support (delivered by ETT or trach):  [ ] Conventional mechanical ventilation  [ ] HFOV    5. If No mechanical ventilation …  [ ] CPAP  [ ] Nasal cannula oxygen  [ ] Face mask oxygen  **Rapid Progression Acute Chest Syndrome Module**  1. Decreased oxygen saturation requiring at least 3 L of oxygen to maintain oxygen hemoglobin saturation at least 90% or intubation and medical ventilator within 24 hours of onset of respiratory symptoms.  [ ] Yes  [ ] No  [ ] Unknown  2. Worsening anemia was arbitrarily defined as a decrease in hemoglobin by ≥ 2 g/dL from baseline.  [ ] Yes  [ ] No  [ ] Unknown  3. Thrombocytopenia (or decrease in platelet count) as defined as a platelet count 150,000/mcl or a 50% decrease from baseline.  [ ] Yes  [ ] No  [ ] Unknown  4. Multiorgan failure (defined as dysfunction of two or more organs by the following criteria [10]: respiratory failure (respiratory distress and at least 3 L of oxygen to maintain oxygen hemoglobin saturation at least 90%), acute renal insufficiency (an increase in the serum creatinine concentration of 50% from baseline; or oliguria of 0.5 mL/kg/hr for more than 6 hours) [17], altered mental status, other neurologic symptoms (new focal neurologic deficit, seizure, confusion, blurred vision), hepatic insufficiency (at least two of the follow features: alanine aminotransferase > 70 U/L, total bilirubin > 2 times upper limit of normal, direct bilirubin > 2 times the upper limit of normal), and prothrombin time prolonged by more than 3 sec [10]. Aspartate aminotransferase was not included because this may be elevated in the setting of hemolysis (Chaturvedi, S., Ghafuri, D. L., Glassberg, J., Kassim, A. A., Rodeghier, M., & DeBaun, M. R. [2016]. Rapidly progressive acute chest syndrome in individuals with sickle cell anemia: distinct acute chest syndrome phenotype. *American Journal of Hematology, 91*(12), 1185–1190).  [ ] Yes  [ ] No  [ ] Unknown |
| **Selection Rationale:** | These questions from the Cure Sickle Cell Initiative (CureSCi) were considered by the Sickle Cell Disease Pregnancy Working Group (WG) to represent the gold standard available to date for collecting details of acute chest syndrome. The WG recommended that this protocol be added to Supplemental Information as the detailed protocol may be too onerous for some studies. |
| **Source:** | Cure Sickle Cell Initiative (CureSCi) Form 4e\_F2910 Acute Chest Syndrome |
| **Availability:** | Available |
| **Life Stage:** | Infant, Toddler, Child, Adolescent, Adult, Senior, Pregnancy |
| **Language:** | English |
| **Participant:** | Participants of all ages with sickle cell disease |
| **Personnel and Training Required:** | Personnel should be trained in medical record abstraction. |
| **Equipment Needs:** | None |
| **General References:** | Ballas, S. K., Lieff, S., Benjamin, L. J., Dampier, C. D., Heeney, M. M., Hoppe, C., Johnson, C. S., Rogers, Z. R., Smith-Whitley, K., Wang, W. C., & Telen, M. J.; Investigators, Comprehensive Sickle Cell Centers. (2010). Definitions of the phenotypic manifestations of sickle cell disease. *American Journal of Hematology*, *85*(1), 6–13.  Bernard, G. R., Artigas, A., Brigham, K. L., Carlet, J., Falke, K., Hudson, L., Lamy, M., Legall, J. R., Morris, A., & Spragg, R. (1994). The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *American Journal of Respiratory and Critical Care Medicine*, *149*(3, Pt. 1), 818–824.<https://doi.org/10.1164/ajrccm.149.3.7509706>  Castro, O., Brambilla, D. J., Thorington, B., Reindorf, C. A., Scott, R. B., Gillette, P., Vera, J. C., & Levy, P. S. (1994). The acute chest syndrome in sickle cell disease: Incidence and risk factors. The Cooperative Study of Sickle Cell Disease. *Blood*, *84*(2), 643–649.  Charache, S., Scott, J. C., & Charache, P. (1979). “Acute chest syndrome” in adults with sickle cell anemia. Microbiology, treatment, and prevention. *Archives of Internal Medicine*, *139*(1), 67–69.  Rackoff, W. R., Kunkel, N., Silber, J. H., Asakura, T., & Ohene-Frempong, K. (1993). Pulse oximetry and factors associated with hemoglobin oxygen desaturation in children with sickle cell disease. *Blood*, *81*(12), 3422–3427.  Stuart, M. J., & Setty, B. N. (1999). Sickle cell acute chest syndrome: Pathogenesis and rationale for treatment. *Blood*, *94*(5), 1555–1560.  Vichinsky, E., Williams, R., Das, M., Earles, A. N., Lewis, N., Adler, A., & McQuitty, J. (1994). Pulmonary fat embolism: A distinct cause of severe acute chest syndrome in sickle cell anemia. *Blood*, *83*(11), 3107–3112.  Vichinsky, E. P., Neumayr, L. D., Earles, A. N., Williams, R., Lennette, E. T., Dean, D., Nickerson, B., Orringer, E., McKie, V., Bellevue, R., Daeschner, C., & Manci, E. A. (2000). Causes and outcomes of the acute chest syndrome in sickle cell disease. National Acute Chest Syndrome Study Group. *New England Journal of Medicine*, *342*(25), 1855–1865. <https://doi.org/10.1056/NEJM200006223422502>  Vichinsky, E. P., Styles, L. A., Colangelo, L. H., Wright, E. C., Castro, O., & Nickerson, B. (1997). Acute chest syndrome in sickle cell disease: Clinical presentation and course. Cooperative Study of Sickle Cell Disease. *Blood*, *89*(5), 1787–1792.  <https://doi.org/10.1056/NEJM200006223422502> |
| **Mode of Administration:** | Medical record abstraction |
| **Derived Variables:** | None |
| **Requirements:** | |  |  | | --- | --- | | **Requirements Category** | **Required (Yes/No):** | | Major equipment | No | | Specialized training | No | | Specialized requirements for biospecimen collection | No | | Average time of greater than 15 minutes in an unaffected individual | No | |
| **Annotations for Specific Conditions:** | None |
| **Process and Review:** | NA |