Review Article

The Impact of Cigarette Smoking and Vaping on Acute Chest Syndrome in Adolescents and Young Adults with Sickle Cell Disease

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ABSTRACT

Sickle Cell Disease (SCD) is a hereditary blood disorder that distorts the shape of red blood cells, increasing the risk of blocked blood vessels and damage to organs. Sickled red blood cells may lead to acute chest syndrome (ACS), which presents with the detection of a lung abnormality during chest imaging accompanied by fever or respiratory symptoms. ACS is a leading cause of premature death in youth with SCD, accounting for one-quarter of SCD-related deaths. For many years, tobacco smoke exposure has been suspected to worsen the frequency or severity of ACS. However, much of the earlier evidence combined children, adolescents, and adults together and relied on self-reported smoking habits. Biomarkers of smoke exposure are now available and e-cigarette use (vaping) has become widespread. The transition period to adulthood is marked by increasing autonomy, experimentation with nicotine products, and peak SCD complications. Therefore, a review of literature discussing the effects of cigarette smoking and vaping in adolescents and young adults with SCD was conducted. Publications were systematically reviewed for the impact of combustible cigarette smoke, second-hand smoke, or vaping in SCD patients ≤24 years old. Across these studies, any tobacco smoke exposure was associated with an increase in ACS- and SCD-related hospitalizations, ACS frequency, ER visits, and overall mortality. This review demonstrates the increased risk for ACS and poor outcomes in the younger SCD population who are at higher risk for experimentation with cigarette smoking and vaping and highlights critical research gaps needed to inform targeted prevention, counseling, and policy interventions.

Keywords: Sickle cell disease; acute chest syndrome; adolescents; cigarette; tobacco smoke; vaping

INTRODUCTION

Sickle Cell Disease (SCD) is a major public health concern. It affects roughly 1 in 365 African American newborns in the United States and over 300,000 infants worldwide each year (1, 2). It is an autosomal recessive genetic disorder caused by a mutation in the β-globin gene located on chromosome 11. This mutation leads to the production of abnormal hemoglobin S (compared to wild-type hemoglobin A), which makes red blood cells deform into a crescent moon (or sickle) shape, especially under low-oxygen conditions. While normal round red blood cells are flexible and smooth and flow more freely through the body's blood vessels, these sickled red blood cells are hard and sticky and can cluster together to clog small blood vessels (vaso-occlusion), resulting in painful

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health emergencies and potential damage to organs (3, 4). Though recent advances in care have improved survival, serious complications are still frequent.

Extended adolescence (approximately 10–24 years of age) is a particularly vulnerable period for individuals with SCD (5). During these years, patients often transition from pediatric to adult healthcare, face new psycho-social stressors, and undergo rapid physiological changes. Notably, teens and young adults with SCD have some of the highest rates of emergency department visits compared to other age groups (6, 7). This age group is also the most likely to start using tobacco or electronic cigarettes (e-cigarettes), also known as vaping. National surveys indicate that a large proportion of high school students experiment with vaping, with over 20% of U.S. 12th graders reporting using an e-cigarette in the past year during 2024 (8). Unfortunately, this means that many adolescents with SCD may be exposed to nicotine and smoke at the very time that their disease complications are peaking.

Acute chest syndrome (ACS) is a severe episode of vaso-occlusion in the lungs characterized by a new pulmonary abnormality (visible as a new opaque marking on a chest X-ray) accompanied by symptoms such as fever, chest pain, coughing, wheezing, or difficulty breathing. It can be triggered by various factors, including lung infections, asthma exacerbations, or an occurrence of fat embolism from the bone marrow. ACS is a relatively common complication in patients with SCD, with up to 50% of children with SCD experiencing at least one episode of ACS at some point in their lives. It is a frequent cause of hospitalization and a major cause of mortality, accounting for about 25% of all SCD-reported deaths (9). Having multiple ACS episodes can lead to lasting lung damage and chronic respiratory problems later in life.

Cigarette smoking and second-hand tobacco smoke have long been thought of as modifiable risk factors for ACS (10). Reports in the early 2000s first suggested that children with SCD exposed to environmental tobacco smoke had worse health outcomes (11). There are various factors that may contribute to a relationship between smoking or tobacco smoke exposure and ACS or the severity of SCD. Smoking is known to cause swelling and inflammation in blood vessels, which narrows the pathway for red blood cells. This, combined with stiff sickled red blood cells that tend to aggregate, increases the risk of ACS and the risk of stroke, heart attack, and death in patients with SCD exposed to cigarette smoke. More recently, however, attention has turned to electronic nicotine delivery systems. Aerosols from vaping devices often contain toxic substances and have been shown to cause e-cigarette or vaping-associated lung injury (EVALI), a condition that clinically resembles ACS in its presentation of acute lung inflammation and respiratory distress in non-SCD patients. As of February 2020, the U.S. Centers for Disease Control and Prevention (CDC) recorded a total of 2,807 reported cases of EVALI (12). Further, 15% of these cases affected people <18 years of age.

Despite these observations, many of the earlier studies on this topic had significant limitations. They often pooled data from adults and children together, making it difficult to identify adolescent-specific effects. They frequently relied on patients or parents to self-report their smoking exposure, which can underestimate true exposure levels. Additionally, most studies did not account for vaping as a source of nicotine and lung injury. Therefore, the aim of this literature review was to perform a targeted analysis of available published data to investigate the impact of cigarette smoke and vaping on the incidence of ACS in adolescents.

METHODS AND MATERIALS

A systematic search of the literature was performed using PubMed and Google Scholar from the creation of each database through April 30, 2025. The search strategy combined keywords and Medical Subject Headings (MeSH) related to “sickle cell disease,” “acute chest syndrome,” “adolescents,” “tobacco smoke,” “second-hand smoke,” “cigarette,” “electronic cigarette,” “vaping,” and “nicotine.” Several inclusion criteria were applied in order to identify and select relevant publications: (1) the report had to be an original research article, review, or case report published in English; (2) the study population was comprised of individuals aged ≤24 years (or the results were stratified by age so that data specific to this age range could be extracted); (3) the study assessed exposure to tobacco in some form—this included active cigarette smoking, second-hand (environmental) tobacco smoke, or use of electronic nicotine delivery systems (vaping); and (4) the study reported pulmonary outcomes, data on ACS incidence or severity, hospitalizations, or mortality.

From each publication that met the above criteria, key data points were considered to assess the overall quality of evidence as well as any potential risk for bias. These included the study design, the number and demographics of participants, the method of assessing smoke or nicotine exposure, and the relevant outcomes measured.

RESULTS

A total of 6 publications were identified which met the above pre-specified inclusion criteria. These consisted of three prospective studies, two retrospective studies, and one study with both a retrospective and prospective monitoring period. Self-reported exposures to tobacco were used in all studies but two also compared these findings to tobacco exposure as measured by salivary cotinine. There were no published studies evaluating the risk of vaping or e-cigarette use in adolescents and young adults with SCD. However, one case report was found that is summarized here as a means for discussion. The key findings from the adolescent and young adult smoking exposure studies are summarized in Table 1.

Impact of Cigarette and Second-Hand Smoke Exposure

Any exposure to tobacco smoke was found to correlate with higher rates of ACS and related complications. In 1992, researchers published data demonstrating an increased incidence of ACS in smokers compared to nonsmokers with SCD (13) (Table 1). They reported unpublished data (Adler S, Scott RB. Unpublished data) from a preliminary study in 1982 that found the hospitalization rate was 1.5 times more frequent for smokers compared to nonsmokers and the rate of pneumonia was 1.25 times higher in smokers compared to nonsmokers. Young and colleagues studied 69 adolescents and young adults (mean age 27 years, 10 were 18 years of age or younger). They found that all 29 smokers had a history of ACS and only 24 of the 37 nonsmokers had a history of ACS (3 were excluded as former smokers) (13).

Second-hand smoke exposure may result in a similar increased risk of ACS. Glassberg and colleagues analyzed ER visit data from 985 children (mean age 9 years old) with SCD (14). They found that living with a household tobacco smoker in the home was associated with a 73% increase in ER visits for acute chest syndrome compared

Table 1. Impact of Cigarette and Second-Hand Smoke Exposure

Authors [Reference #]	Design	N	Age Range	Exposure Measure	Key Findings
Young et al., 1992 (13)	Prospective	69	Adolescents and young adults (10% 18 yrs old or younger)	Self-reported	ACS frequency higher than expected in smokers (all 29 smokers had ACS) and lower than expected in nonsmokers (24 of the 37 had ACS)
West et al., 2003 (11)	Retrospective	52	2-18 yrs old	Self-reported	Mean number of hospitalizations and hospital days related to sickle cell crises in smoke exposed patients compared to non-exposed over 2 year period (3.7 hospitalizations compared to 1.7, 23.4 days compared to 9.3)
Glassberg et al., 2013 (14)	Prospective	985	5-14 yrs old	Self-reported	Tobacco smoke home exposure associated with 73% more ER visits for ACS compared to non-exposed
Sadreameli et al., 2015 (15)	Retrospective for 2 years, prospective for 15 months	49	IQR: 5-15 yrs old, median age 9.3 yrs old	Self-reported, salivary cotinine level	Smoke exposed patients with Incidence Rate Ratio 3.7 for all hospitalizations, 4.3 for hospitalizations for pain crises, and 5.7 for hospitalizations for ACS compared to non-exposed
Tackett et al., 2019 (16)	Retrospective	27	Median age: 9 yrs old; SD: 4.5 yrs old	Self-reported, salivary cotinine level	88% of cohort was positive for smoke exposure, no associations between cotinine levels and ER utilization, sickle cell crises, or pulmonary function
Knight- Madden et al., 2013 (17)	Prospective	75	19-27 yrs old	Self-reported	Smokers had a mortality Hazard Ratio of 2.7 over 10 yr period

IQR = Interquartile Range; SD = Standard Deviation.

to those without household exposure (RR 1.73, 95% CI = 1.09 to 2.74). A retrospective study conducted in 2003 reported that children with SCD who were exposed to cigarette smoke or environmental tobacco smoke in the home had substantially worse outcomes than those who were not exposed (11). In that study, 52 patients aged 2-18 years old with SCD were analyzed and 22 (42%) were found to have environmental tobacco smoke exposure. The study found that exposure to environmental tobacco smoke was associated with about a 2-fold increase in sickle cell crises (mean 3.7 events during the 2-year period compared to 1.7 events in the patients not exposed to smoke) and an increase in total number of hospital days for ACS compared to unexposed children (mean 23.4 days compared to 9.3 days).

While most studies evaluating smoke exposure used self-reporting to track smoke exposure, a U.S. cohort study by researchers at Johns Hopkins University objectively measured tobacco exposure using salivary cotinine (a metabolite of nicotine) in 49 children and young adults with SCD (15). They found that nearly half (22) of the participants had significant evidence of tobacco smoke exposure, and those with salivary cotinine levels ≥0.5 ng/mL had a greater than 3-fold increased risk of hospitalization and greater than 5-fold increased risk of emergency department visits than those without smoke exposure. Significantly, they found, when compared to salivary cotinine levels (objective measure), their questionnaire (subjective) was 62.5% sensitive, and 75% specific and physician documentation of smoke exposure was only 31.8% sensitive and 100% specific. More recently, Tackett and colleagues also used salivary cotinine in addition to exhaled carbon monoxide to assess smoke exposure in SCD patients (16). They found the majority of their population sample (24 of 27 participants, 88%) demonstrated second-hand smoke or vape exposure by cotinine analysis. Interestingly, they did not identify any association between smoke or vape exposure and health care utilization, pulmonary function, or disease severity. This may have been due to the limited sample size or missing health record information. They, too, found that caregiver-reported second-hand smoke or vape exposure was a poor indicator of actual smoke or vape exposure when measured by objective means. Therefore, future research evaluating the effects of smoke or vape exposure may benefit from objective biomarker data for improved accuracy. Furthermore, additional data analyses comparing the quantitative values of these biomarkers across larger populations and multiple studies may provide useful insight in identifying specific age groups or other covariates that may significantly influence clinical outcomes, including mortality.

Lastly, a longitudinal study published in 2013 and conducted over 10 years followed 75 SCD patients (aged approximately 19-27 years) and found that smokers had a 2.7 times greater risk of death compared to nonsmokers (17).

Vaping and Electronic Nicotine-Delivery Systems

Studies evaluating the risk of ACS due to e-cigarette or vape use in patients with SCD were not found in this literature review. This may be due to the relatively recent nature of the rise of e-cigarette use. Given the rampant rise of vaping and its prevalent abuse by the current generation of adolescents and young adults, this is a notable cause for concern in patients with SCD. Adolescents were prominently affected during the outbreak of e-cigarette or vaping-associated lung injury (EVALI) that peaked in 2019. Most patients hospitalized in the 2019–2020 EVALI epidemic were teenagers and young adults (18). While the mechanism for lung injury in EVALI is different than ACS, the clinical features of EVALI in youth, such as coughing, chest pain, shortness of breath, and diffuse lung opacities on imaging, mimic the presentation of ACS. This poses a serious diagnostic challenge in any adolescent with SCD who vapes.

One case report published in 2023 was identified regarding a 21-year-old woman with SCD who presented with vaso-occlusive pain after using an e-cigarette for the first time (19). She presented with severe rib and back pain worsening over 4 days. She required oxygen supplementation and pain medications in the ER and during her hospital admission. While this did not seem to be an ACS episode (chest X-ray did not show signs of ACS), ACS is known to be a vaso-occlusive event so it may signal a possible increased risk for ACS with e-cigarette use.

There are reasons to suspect that vaping could be as dangerous as or even more dangerous than traditional cigarette smoking for individuals with SCD. Vaping devices produce an aerosol containing nicotine, ultrafine particles, heavy metals, and volatile aldehydes (like formaldehyde and acrolein). In lung cell and animal studies, these have been shown to generate reactive oxygen species and cause inflammation and endothelial dysfunction. Patients with SCD are already known to have some baseline inflammation and endothelial problems. For example, their blood vessels tend to have higher adhesion molecule expression and impaired nitric oxide signaling due to the sickling process. The toxic

chemicals in e-cigarette vapor can further exacerbate these vulnerable pathways, potentially triggering vaso-occlusion or lung injury.

Given that vaping is widespread among teens and mistakenly often perceived as harmless, these findings highlight a potential public health crisis. Public health data show that a substantial fraction of teenagers are using e-cigarettes regularly (8), suggesting that many adolescents and young adults with SCD may unknowingly be exposing themselves to these risks. We believe physicians should proactively inquire about vaping in SCD patients and treat it as a serious potential trigger for ACS.

DISCUSSION

In concordance with earlier literature, this updated review affirms that exposure to cigarette smoke substantially increases the risk and severity of acute chest syndrome in young people with SCD. This aligns with findings in the adult population. A 2013 publication by researchers collaborating across eight universities primarily within the U.S. reported that adult SCD smokers had significantly higher odds (RR 2.61) of experiencing ACS or severe pain events compared to nonsmokers (10).

Cigarette smoke introduces a variety of harmful agents into the airways and bloodstream. This increases the production of free radicals, such as reactive oxygen species and reactive nitrogen species, which can lead to tissue damage and inflammation. Chemicals contained in cigarette smoke can activate signaling pathways in endothelial cells lining blood vessels that can result in increased stickiness of the blood vessel lining, making them prone to vaso-occlusion (20). The combination of smoking-induced injury and the risk for vaso-occlusion with sickle-shaped red blood cells in patients with SCD may explain the higher risk for ACS found in this review of the literature. Many adolescents with SCD also have co-existing asthma or other lung conditions, which further elevate their risk for ACS. Smoke exposure in such cases is especially dangerous, since it can trigger asthma attacks in addition to causing sickling events. For example, it was found that children with SCD exposed to environmental tobacco smoke (ETS) early in life (during infancy and preschool period) were more likely to have airway obstruction on pulmonary function testing (21). They were also more likely to respond to bronchodilators on the same pulmonary function test. ETS was also associated with increased frequency of cough and wheezing with exercise and more frequent awakening during sleep.

Although e-cigarette use has not been well studied in this population, there is burgeoning evidence that vaping should be viewed with similar concern. E-cigarette vapor creates a toxic environment in the lungs that is rich in ultrafine particles, chemical irritants, and nicotine. The inflammatory response and tissue injury from these inhaled substances may be just as harmful as those caused by traditional cigarette smoke. Vaping might pose unique risks, as it is known that certain oils or additives found in e-cigarette liquids can cause severe lung damage (as seen in EVALI cases). For clinicians, a vaping-related lung injury can present very similar to ACS in a patient with SCD with symptoms of chest pain and difficulty breathing. This overlap means that doctors must screen for vaping when evaluating SCD patients with acute respiratory symptoms to ensure proper management (e.g., corticosteroids may need to be considered to treat EVALI). No studies distinguished any safe level of tobacco smoke or e-cigarette vapor exposure. Unlike some risk factors that might have a threshold, even occasional smoking or vaping could potentially trigger serious events. This underscores the need for immediate attention and public health awareness to promote avoidance of tobacco and e-cigarette products in this high-risk group.

Given the significant prevalence of smoke exposure found in young patients with SCD and the known association with increased complications of SCD, it would be important to consider adding screening for smoke exposure to the routine care of patients with SCD. While our research showed that self-reporting was not as accurate as salivary cotinine evaluations to determine smoke exposure, adding screening questions about smoking, e-cigarette use, and exposure to smoke and e-cigarettes in the patient's environment would be relatively easy for all SCD clinicians to implement. Current treatment guidelines for the care of patients with SCD could be amended to include this recommendation. The addition of salivary cotinine screening may be limited by the availability of accurate testing and cost of such a screening test. However, it may be beneficial to consider salivary cotinine as a secondary screening test in patients who have frequent acute chest episodes but deny significant exposure to tobacco smoke or e-cigarettes by self-report, given the evidence showing the somewhat poor sensitivity of self-reporting or physician documentation of smoke exposure when compared to an objective measure of nicotine exposure (salivary cotinine).

There are several limitations to the existing studies

that should be acknowledged. Many studies had small sample sizes, which can limit the statistical power to detect effects or subgroup differences. The same Johns Hopkins University researchers mentioned earlier found discordance between self-reported tobacco smoke exposure and salivary cotinine levels indicating research based on self-reported tobacco smoke exposure alone may be inaccurate (22). Medication use (like hydroxyurea, which can reduce SCD complications), the presence of comorbid conditions (like asthma), and demographic differences (e.g. neighborhood, proximity to freeways) may also affect the incidence of SCD complications and not all studies were able to control for these variables. Additionally, it was noted that longitudinal data on lung function were not studied.

Future research should prioritize prospective cohort studies that follow a large group of adolescents and young adults with SCD, periodically measure their exposure to tobacco smoke (including second-hand smoke and vaping) through objective biomarker tests and track their health outcomes over time. They also may include objective measures of lung function, like periodic pulmonary function tests, to track changes in lung function. These types of studies may have a better chance at establishing a clear exposure-response relationship and potentially identify a valid threshold cutoff that reflects significantly increased clinical risk. Including vaping in any assessment is crucial, particularly given how common e-cigarette use is among today's youth.

It will also be important to investigate the potential reversibility of these adverse clinical impacts following cessation of tobacco smoke exposure and vaping. Controlled trials might explore specific interventions (such as smoking cessation programs or medications like nicotine patches) in adolescents and young adults with SCD to evaluate success rates and whether that translates into fewer SCD complications. Following SCD patients who are smokers after quitting or removing smoke exposure and documenting changes in ACS events and other SCD complications could evaluate the effectiveness of anti-smoking/vaping interventions and inform clinical guidelines.

Beyond research, this review carries some practical implications for healthcare providers and families. Physicians and nurses caring for adolescents and young adults with SCD should be proactive in discussing smoking and vaping at every opportunity. Regular screening for tobacco exposure (both cigarettes and e-cigarettes) in clinic visits or hospital admissions can help identify at-risk patients. Given the strong evidence that avoiding smoking can improve outcomes, counseling should emphasize how smoking or vaping could directly lead to an ACS episode or a pain crisis. Such counseling should aim to be delivered in a teen-friendly manner. Healthcare providers might also consider using mobile health tools, such as smartphone apps or text-messaging programs, to engage teens in quitting smoking or vaping. These tools can send reminders, motivational messages, or useful tips for dealing with peer pressure and cravings. These strategies would help to make the quitting process more interactive and relatable for the younger population.

Another important factor in the prevention of smoke exposure is peer and family support in the cessation process. Support groups or mentoring programs could pair SCD patients with a peer who has managed to quit smoking, allowing them to share experiences and coping strategies.

By implementing these supportive interventions and leveraging teachable moments (e.g. an ACS hospitalization as an opportunity to discuss quitting), healthcare providers can guide teens and young adults with SCD toward healthier choices. The ultimate goal is to reduce or eliminate smoke exposure, which in turn could lead to fewer ACS episodes and better overall outcomes for those living with SCD.

CONCLUSION

Cigarette smoking, second-hand tobacco smoke exposure, and vaping all seem to carry a significant risk of ACS and other SCD complications for adolescents and young adults with sickle cell disease. Prevention, screening, and cessation programs should be widely implemented and integrated into the routine care of young SCD patients to help keep them free of tobacco smoke and e-cigarette exposure. This might include regular screening for tobacco smoke and e-cigarette/vaping exposure as well as counseling about the dangers of smoking/vaping. It would also be important to discuss and provide helpful resources to quit. From a public health perspective, policies that limit youth access to tobacco and e-cigarettes and that promote smoke-free environments are especially important for families affected by SCD. Well-designed prospective studies focusing on adolescents and young adults with SCD are vital to better establishing a causative relationship between smoke/e-cigarette exposure and ACS. Such research will help clearly define and optimize existing clinical guidelines and inform evidence-based public health policies aimed at eliminating smoke exposure in this high-risk population.

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