RESEARCH PAPER

Coagulation Disorders in Cyanotic Congenital Heart Diseases: Surgical Implications

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ABSTRACT

Background:

Cyanotic congenital heart disease (CCHD) is an intricate congenital heart problem characterized by the passage of deoxygenated blood into the systemic circulation without passing through the lungs, resulting in chronic hypoxemia. In response, there is an increase in the number of red blood cells (secondary polycythemia), which causes the thickening of the blood and an imbalance in the normal processes of blood clotting. Thus, patients with CCHD are prone to develop both thrombosis and hemorrhage. Typical disorders include low platelets, dysfunctional platelets, low coagulation factors, enhanced fibrinolysis, and acquired von Willebrand disease. Performing surgery on such a patient, particularly when cardiopulmonary bypass is used, will further aggravate these problems due to hemodilution, inflammatory responses, and platelet activation.

Objective:

For analyzing the pathophysiology of coagulation abnormalities in patients with cyanotic congenital heart disease, studying the various diagnostic tools used in assessing these diseases, and understanding the current management techniques of such patients during surgery using cardiopulmonary bypass is essential.

Methods:

This systematic review analysed published clinical studies, observational research, trials, and reviews on coagulation disorders in CCHD patients undergoing surgery. Parameters assessed included haemoglobin, haematocrit, platelet count, PT, INR, aPTT, fibrinogen, and D-dimer. Point-of-care tests such as TEG and ROTEM were also reviewed. Intraoperative factors including CPB management, anticoagulation monitoring, and blood conservation methods like modified ultrafiltration and cell saver were evaluated. Preoperative optimization strategies such as correction of iron deficiency, thrombocytopenia management, and venesection for severe polycythaemia were also examined.

Result:

Patients with CCHD showed clear coagulation abnormalities even before surgery. Common findings included raised haematocrit, thrombocytopenia, prolonged PT, INR, and aPTT, low fibrinogen levels, and deficiencies of clotting factors. Platelet dysfunction was also present in some patients despite normal platelet counts. During surgery, heparin resistance was frequently observed because polycythaemia reduced plasma volume, requiring higher heparin doses to achieve target ACT. After surgery, these patients had increased chest tube bleeding, higher blood transfusion requirements, more re-exploration procedures, and serious complications such as disseminated intravascular coagulation (DIC). The severity of abnormalities increased with higher polycythaemia, longer duration of cyanosis, and advanced pulmonary vascular disease. TEG- and ROTEM-guided transfusion strategies were more effective than empirical treatment in reducing blood product use and improving outcomes.

Conclusion:

Coagulation disorders in CCHD are multifactorial and clinically important. Effective management requires preoperative hematological assessment, careful intraoperative perfusion strategies with modified ultrafiltration and tranexamic acid, and postoperative viscoelastic monitoring. A multidisciplinary team is essential to balance the risks of thrombosis and bleeding in these patients.

KEY WORDS: Cyanotic congenital heart disease, Polycythemia, Coagulation disorders, Cardiopulmonary bypass,

Hypoxemia, Thrombocytopenia, Thromboelastography, Hemostasis, Surgical implications
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INTRODUCTION

The cyanotic congenital heart disease (CCHD) is a serious medical condition that poses huge health challenges, particularly in developing nations such as India, which are characterized by late detection of this condition. This refers to congenital heart anomalies that lead to the movement of deoxygenated blood from the right side of the heart to the left side through right-to-left shunts. The most common examples include Tetralogy of Fallot, Transposition of the great arteries, Tricuspid atresia, pulmonary atresia, and single ventricle heart with pulmonary stenosis.[1]

The pathological process begins with chronic arterial oxygen desaturation, which stimulates increased erythropoietin production by the kidneys. This causes secondary erythrocytosis, increasing red blood cell mass to improve oxygen transport.[2] Although compensatory, it progressively raises blood viscosity and creates challenges during surgery. Thickened blood leads to vascular stasis and sluggish microcirculation. Increased shear stress activates platelets and the coagulation cascade, resulting in chronic low-grade consumption coagulopathy. [3,4] At the same time, chronic hepatic hypoperfusion caused by prolonged hypoxemia reduces the liver's ability to produce clotting factors, especially the vitamin K-dependent factors II, VII, IX, and X.

The haemostatic profile in CCHD is paradoxical and clinically challenging. Hyperviscous blood increases the risk of thromboembolism, while platelet consumption, qualitative platelet dysfunction, and reduced coagulation factor levels increase bleeding tendency.[5] This dual risk is further worsened by acquired von Willebrand syndrome, where high-velocity flow across intracardiac defects damages large von Willebrand factor multimers needed for primary haemostasis.[6] Studies have shown that the severity of these abnormalities is directly related to the degree of polycythaemia and the duration of cyanosis.[5,6,7] Tetralogy of Fallot is the commonest form of cyanotic congenital heart disease with an incidence of 1/3500 and represents 7 to 10 percent of all cases of congenital heart defects.[8] Those who do not undergo surgery have poor prognoses, with less than 10 percent surviving for 21 years post birth.[9,10,11] In developing nations, those who present with late symptoms are in a different category altogether since they exhibit signs of polycythaemia, severe haemostatic disturbances, and a high surgical risk.[12]

The management of coagulation disorders in patients with CCHD is one of the main problems that surgeons face. If such a patient goes through surgery using the cardiopulmonary bypass (CPB), the already dysfunctional haemostasis will be under even more stress due to haemodilution secondary to CPB priming, systemic inflammation due to contact with artificial materials, mechanical activation and consumption of platelets, and depletion of the coagulation factors.[13,14] All these aspects can have a significantly adverse effect on pre-existing disorders and cause surgical bleeding. Hence, proper early identification, accurate prediction, and adequate preparation for haemostasis disorders are critical in order to improve outcomes in these patients.

2. MATERIALS AND METHODS

2.1 Study Design

The management of blood clotting disorders in cases of congenital heart disease is an important problem in surgery. Under the conditions of cardiac surgery with CPB, haemostasis disorder is exacerbated by dilution, systemic inflammatory response caused by the contact of blood with artificial surfaces, platelet activation and destruction, and deficiency of coagulation factors. Such conditions may increase preexisting disturbances and cause profuse bleeding.

2.2 Literature Search Strategy

The management of blood clotting disorders in cases of congenital heart disease is an important problem in surgery. Under the conditions of cardiac surgery with CPB, haemostasis disorder is exacerbated by dilution, systemic inflammatory response caused by the contact of blood with artificial surfaces, platelet activation and destruction, and deficiency of coagulation factors. Such conditions may increase preexisting disturbances and cause profuse bleeding.

2.3 Inclusion and Exclusion Criteria

Inclusion Criteria

- Studies involving patients diagnosed with cyanotic congenital heart disease of any age (neonates to adults with persistent cyanosis).
- Original research articles, observational studies, cross-sectional studies, and clinical trials reporting on coagulation parameters or hemostatic outcomes.
- Relevant systematic reviews documenting coagulation

parameters, platelet function, or clinical coagulopathic outcomes in CCHD patients.

Exclusion Criteria

- Studies related exclusively to acyanotic congenital heart disease.
- Articles not reporting on coagulation or hemostatic parameters.
- Studies involving patients on established anticoagulant or antiplatelet therapy prior to enrollment.
- Studies without relevant coagulation outcome data.

2.4 Clinical Assessment Parameters

All patients undergoing surgical correction of cyanotic congenital heart disease underwent detailed preoperative haematological evaluation including CBC with haemoglobin, haematocrit, platelet count, peripheral smear, PT/INR, aPTT, fibrinogen, liver and renal function tests, arterial blood gas analysis, and TEG/ROTEM when indicated for clot assessment. Patients with haematocrit >65% were considered for venesection with isotonic saline infusion to reduce blood viscosity. During CPB, ACT was monitored every 30 minutes. Modified ultrafiltration was performed after bypass when appropriate . Postoperative PT/INR, aPTT, fibrinogen, and platelet counts were repeated at 6, 12, and 24 hours, with transfusion guided by TEG/ROTEM.

2.5 Perfusion Equipment and Circuit

The cardiopulmonary bypass circuit consisted of a heart-lung machine with roller or centrifugal pump, membrane oxygenator with reservoir and heat exchanger, PVC tubing, arterial filters, bubble traps, haemoconcentrator, ACT monitor, and blood gas analyser. Standard aortic and bicaval venous cannulation was used. Cardioplegia was given using St. Thomas or Del Nido solution. Prime fluid included Ringer's lactate, normal saline, colloids, and fresh frozen plasma in CCHD patients to reduce dilutional coagulopathy. Cell saver devices were used for autotransfusion. Heparin 300–400 IU/kg maintained ACT >480 seconds, followed by protamine reversal after bypass.

3. PATHOPHYSIOLOGY OF COAGULATION DISORDER

Pathophysiology of CCHD coagulopathy is a multifaceted series of physiological processes that occur as a result of continuous systemic hypoxemia. In the end, it results in a haemostatic disorder that is both unique and dangerous for surgical purposes.

3.1 Secondary Erythrocytosis and Hyperviscosity

Chronic arterial oxygen desaturation increases erythropoietin production by the kidneys, leading to secondary erythrocytosis and expansion of red blood cell mass.[2] Although this improves oxygen transport, it markedly raises blood viscosity. Thickened blood causes vascular stasis with slow microvascular flow and abnormal shear stress on the endothelium.[3] This stress activates platelets and the coagulation cascade, resulting in chronic low-grade consumption coagulopathy, where platelets and clotting factors are gradually depleted.[4]

3.2 Thrombocytopenia and Platelet Dysfunction

Thrombocytopenia is a common preoperative finding in CCHD patients due to shortened platelet survival from turbulent intracardiac flow and microvascular stasis. Platelet counts are often inversely related to haematocrit levels.[1,15,16], In addition to low counts, qualitative platelet dysfunction is significant. Impaired platelet adhesion, aggregation, and activation may occur even with near-normal platelet counts.[17] Chronic hypoxemia also causes excess platelet microparticle production, indicating continuous activation and exhaustion, while platelet factor III activity is significantly reduced.[18]

3.3 Coagulation Factor Deficiency

The liver, with chronic hypoxia and congested veins of the liver, gradually becomes unable to produce clotting factors that are dependent on vitamin K, such as Factors II, VII, IX, and X. Although vitamin K is naturally produced in the body by bacteria and absorbed, the process of conversion from precursor clotting proteins to functional clotting factors requires the enzymatic activity of the liver that becomes deficient in hypoxic states.[19]

3.4 Disseminated Intravascular Coagulation and Fibrinolysis

The polycythemia associated with CCHD causes thickening of the blood and thus poor microcirculation and perfusion of tissues. The end result is vascular stasis, which leads to the development of fibrin and platelet clots, resulting in consumptive coagulopathy, similar to that seen in DIC. Primary fibrinolysis has also been noted, with an increase in plasminogen activators and a decrease in the activity of antiplasmin, which results in constant bleeding.[20]

4. PATHOPHYSIOLOGIC CHANGES OF CHRONIC HYPOXEMIA IN THE HAEMOSTATIC SYSTEM

4.1 Polycythaemia and Its Haemostatic Consequences

Chronic cyanosis in conditions such as Tetralogy of Fallot causes increased erythropoietin production, leading to compensatory erythrocytosis. As haematocrit rises, blood

viscosity increases, reducing microcirculatory perfusion and causing endothelial shear stress.[21,22] Erythrocytosis may be compensated, with haematocrit usually below 65%, or decompensated, where persistent erythropoietin release causes rising haematocrit, oxygen saturation below 75%, and symptoms of hyperviscosity such as headache, fatigue, myalgia, paraesthesia, and poor mentation.[23,24] Iron-deficient cyanotic patients are at higher risk because microcytic rigid red cells further worsen viscosity despite lower red cell mass.[21]

4.2 Hemostatic Abnormalities Related to Hypoxemia

Patients with chronic hypoxemia-related CCHD have a significant bleeding tendency due to multiple haemostatic abnormalities. These include thrombocytopenia, impaired platelet function, shortened platelet survival, excess platelet microparticles, reduced clotting factor synthesis, excessive fibrinolysis, and low-grade disseminated intravascular coagulopathy.[25,26,27,28,29,30] Severity usually increases with greater polycythaemia, and haematocrit is often inversely related to platelet count.[5,6,7] During cardiopulmonary bypass, these problems worsen further because of haemodilution, clotting factor loss, and platelet activation or consumption.[31,32]

4.3 Role of Chronic Hypoxemia in Coagulation Factor Synthesis

Chronic hypoxia causes a gradual decrease in liver synthetic capability among patients with CCHD. The factors that are dependent on the vitamin K cycle are clotting factors II, VII, IX, and X, which are synthesized by the liver. As a result of the constant congestion of the liver due to high pressure on the right side, these clotting factors are inadequately formed and activated. Despite vitamin K administration, these clotting factors still cannot be adequately formed, implying that there is an intrinsic problem with liver synthesis. During surgery, other factors like surgical trauma, hemodilution, heparinization, and inflammation during cardiopulmonary bypass may aggravate this issue.[19]

5. SURGICAL IMPLICATIONS OF COAGULATION DISORDERS

Coagulation abnormalities in CCHD create a series of specific and serious surgical challenges during both the operative and postoperative periods. A thorough understanding of these implications is essential for every member of the cardiac surgical team.

5.1 Preoperative Surgical Preparation

All CCHD patients should be regarded as high-risk for hemostatic complications prior to any surgical planning. Preoperative assessment must include a comprehensive coagulation panel: platelet count and functional assessment, PT/INR, aPTT, fibrinogen, liver function tests, and where available, TEG or ROTEM. Correction of iron deficiency anemia should be undertaken before surgery, as iron deficiency worsens microcyte rigidity and blood viscosity.[21,33] In patients with hematocrit exceeding 65% and symptomatic hyperviscosity, therapeutic venesection with simultaneous isotonic volume replacement (500 ml over 30 to 45 minutes) is recommended, as this has been shown to significantly reduce intraoperative blood loss and postoperative complications. Preoperative vitamin K supplementation is indicated to partially correct factor deficiency from chronic hepatic congestion.[19]

4.2 Intraoperative Management Challenges

Intraoperatively, heparin resistance due to the presence of increased plasma protein levels and low plasma volume in polycythaemia constitutes a significant issue. Usual heparin dosing (300–400 IU/kg) may prove insufficient, hence regular assessment of the activated clotting time (ACT) every 30 minutes becomes crucial, and heparin should be administered if needed.[36] Anti-Xa level measurement might be helpful for patients with high haematocrits, where the ACT alone might overestimate anticoagulation levels.[27] Intraoperative bleeding is expected to exceed that seen in acyanotic patients, requiring more fresh frozen plasma (FFP), platelets, cryoprecipitate, and packed red blood cells.[34]

4.3 Postoperative Hemostatic Complications

The postoperative period is the most critical phase of haemostatic risk in CCHD patients. They often have higher chest tube drainage, increased re-exploration for bleeding, longer ICU stay, and sometimes DIC. Platelet function is lowest during the first 48 hours after CPB, making this the highest-risk period for bleeding.[35] TEG/ROTEM-guided transfusion is superior to empirical therapy because it allows targeted correction of specific deficiencies. Early detection of falling platelets, raised INR, low fibrinogen, and increased chest tube output is essential. Desmopressin (DDAVP) may help patients with platelet dysfunction or acquired von Willebrand syndrome.[36]

5. RESULTS

5.1 Preoperative Coagulation Profile

Studies published confirm hemostatic alterations in CCHD patients prior to surgery. Polycythemia is the most common abnormality, with hematocrit in the range 55–72% in severe cases, particularly in Eisenmenger syndrome. This leads to dual risk of thrombotic complications because of hyperviscosity and hemorrhagic due to thrombocytopenia and platelet dysfunctions.[35]

Thrombocytopenia was commonly reported, with platelet count varying between 60,000 and 140,000/mm³ depending on the severity of disease.[6] Saqlain et al. reported thrombocytopenia in 48% of children, prolongation of PT in 56%, increase in INR in 43%, and prolonged aPTT in 36%.[40] Thrombocytopenia was reported by Mishra et al. in 19.4% of cases, more frequent in TAPVC.[41] Abnormalities in PT, aPTT, and platelet count were seen in over 70% of cyanotic patients by Colon-Otero et al., predicting increased intraoperative bleeding.[26]

Even patients with normal platelet counts were shown to have qualitative dysfunction of platelets. It was observed that platelet aggregation and adherence were significantly compromised in cyanotic children; this was associated with chronic hypoxemia, increased shear stress, and endothelial dysfunction.[18] Reduced platelet adhesiveness and platelet factor III activity was described by Bhargava et al., who associated these qualitative abnormalities with hemorrhagic tendencies seen in cyanotic patients, even with minimal thrombocytopenia.[20] Vitamin K-dependent factors, including Factors II, VII, IX, and X, were described as being impaired due to impaired hepatic production of these factors, which was evidenced by the finding that even after administration of vitamin K, the deficiencies remained unaltered.[21] Elevated d-dimers were found in many cyanotic patients, which is indicative of compensated DIC with active thrombin formation and fibrinolysis.[42]

5.2 Intraoperative Findings

There were several publications that have demonstrated that hemostatic stress increases significantly in CCHD patients following the onset of CPB. The resistance to heparin was often observed in cyanotic children where they required larger doses of heparin to maintain ACT > 480 s compared to acyanotic counterparts. In a study conducted by Bhardwaj et al. involving 60 cyanotic patients versus 30 non-cyanotic subjects, lower clot strength, delay in clot formation, and enhanced fibrinolysis was detected using TEG, ROTEM, and Sonoclot assays.[28]

The incidence of surgical blood loss in cyanotic patients was consistently high. As reported in another study carried out by Chauhan et al. involving 75 CCHD patients who were randomized into aprotinin, epsilon-aminocaproic acid, and control groups, a mean amount of 780 ml of blood was lost in controls while only 460-510 ml was lost after anti-fibrinolytic treatment, reflecting a 35-40% reduction.[33] The utilization of FFP, platelets, cryoprecipitate, and packed red cells was significantly higher than in acyanotic controls. Modified ultrafiltration post-CPB led to less need for transfusion and hemostatic improvement in those centers that were employing this method regularly.[28]

5.3 Postoperative Outcomes

Postoperative phase in CCHD patients poses a higher risk of haemostatic problems compared to acyanotic patients. According to Gomes and McGoon, there were three times more chest tube drainage in the first 12 hours, reoperation rate of 12.5% compared to 3.8%, and mortality of 10.4% compared to 4.2%.[37] The most common cause of reoperations was the occurrence of coagulation disorder rather than excessive bleeding from surgical site. Coagulation function is impaired even more in the first 48 hours after surgery, usually recovering within 7-10 days.[38]

Another severe complication observed in the study was disseminated intravascular coagulation (DIC). DIC manifested itself with progression of thrombocytopenia, hypofibrinogenemia, and uncontrollable bleeding regardless of transfusions. Coagulopathy was an independent prognostic factor for mortality.[6] Transfusion based on TEG- and ROTEM-based criteria proved to be more effective than empirical approach. It resulted in decreased need for transfusion, reduced length of stay at intensive care unit and less complications.

DISCUSSIONS

Earlier studies by Jackson and Ekert and Gilchrist were among the first to identify a significant bleeding tendency in cyanotic congenital heart disease (CCHD) patients, attributing it to polycythaemia-driven platelet dysfunction and coagulation factor depletion.[1,5] Wedemeyer et al. further confirmed that haemostatic abnormalities worsened proportionally with rising haematocrit, and Goldschmidt demonstrated that vitamin K-dependent factor deficiencies persisted despite supplementation, pointing to impaired hepatic synthesis.[17,21] These foundational observations established the clinical framework for perioperative coagulation management in CCHD.

In contrast, more recent investigations have refined both diagnostic and therapeutic approaches considerably. Bhardwaj et al. demonstrated that standard laboratory tests such as PT and aPTT consistently underestimated the true haemostatic deficit, whereas viscoelastic modalities — TEG, ROTEM, and Sonoclot — simultaneously revealed reduced clot strength and hyperfibrinolysis during

cardiopulmonary bypass.[28] Williams et al. formally quantified the paradoxical dual haemostatic hazard of simultaneous thrombotic and haemorrhagic risk, while Saqlain et al. confirmed in a contemporary paediatric cohort that thrombocytopenia and coagulation factor deficiencies remain prevalent even today.[35,40] Collectively, the evidence demonstrates that while the underlying pathophysiology recognized by early investigators remains unchanged, modern management must integrate point-of-care functional coagulation testing and individualized, goal-directed blood product therapy to meaningfully reduce surgical morbidity in this complex patient population.

SUMMARY

The present systematic review analyzed the coagulation disturbances in the patients with cyanotic congenital heart diseases and the impact of these disturbances on the surgical outcomes during cardiopulmonary bypass. The published data on the changes in hemostasis in patients with CCHD at preoperative, intraoperative and postoperative period have been evaluated.

Preoperative assessment demonstrated polycythemia with the high level of hematocrit as the most frequent finding among patients with CCHD. In some patients there were signs of thrombocytopenia and qualitative disturbances in platelet function despite normal platelet count. Prothrombin time, INR and aPTT were prolonged that is associated with the synthesis inhibition of coagulation factors caused by chronic hypoxia. Low levels of fibrinogen and fibrinolysis in the patients were identified as well.

During intraoperative period the patients with CCHD needed larger doses of heparin due to heparin resistance connected with polycythemia. Increased blood loss, need for high volumes of FFP, platelets, cryoprecipitate and packed red blood cells has been found out in CCHD group. The use of modified ultrafiltration during CPB contributed to the reduction of blood transfusion and to the restoration of hemostasis. Preoperative venesection in patients with hematocrit more than 65% contributed to the lower intraoperative blood loss and improves post operative coagulation parameters.

The postoperative period was characterized by an increased incidence of profuse chest drain output, re-exploitation due to excessive blood loss, prolonged intensive care unit stays, and in worst-case scenarios, disseminated intravascular coagulation in patients with CCHD. Mortality risk was greatest for those patients who had severe pulmonary vascular involvement, inadequate coagulation prior to surgery, and uncontrolled postoperative bleeding. Protocols based on TEG and ROTEM transfusions were found to be more advantageous than empiric management. Coagulation disturbances were directly proportional to the extent of polycythemia, time duration of cyanosis, and pulmonary vasculature remodeling. Multidisciplinary teamwork by cardiac surgeons, anesthesiologists, cardiac perfusionists, intensivists, and hematologists was always considered a key aspect of successful patient care.

CONCLUSION

Cyanotic CHD patients with coagulation abnormalities exhibit multiple causative factors, predictable outcomes, and clinical relevance, thus putting them at high risk for hemostatic problems during the operation. Preoperatively, there must be an effort toward complete patient optimization by correcting iron deficiency, thrombocytopenia, coagulopathy, venesection of hematocrit greater than 65%, and giving vitamin K. During surgery, the use of increased heparinization, close observation of ACT values, appropriate priming of CPB circuit, modified ultrafiltration technique, and cell saver technology will ensure hemostasis. TEG/ROTEM evaluation on a regular basis enables early detection of coagulation abnormalities and provides timely targeted blood transfusion. Postoperatively, it is critical to monitor platelets, INR, fibrinogen, and chest tube output to determine coagulation failure. The use of additional agents such as tranexamic acid and desmopressin is useful.

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