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REVIEW ARTICLE

SYSTEMATIC REVIEW ON AFIBRINOGENAEMIA

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Abstract

Congenital afibrinogenemia is a bleeding disorder caused by a blood clotting disorder. Normally, blood clots protect the body after an injury by blocking damaged blood vessels and preventing further blood loss. However, bleeding is uncontrolled in patients with congenital afibrinogenemia. Newborns with this condition often have prolonged bleeding from the umbilical cord stump after birth. Nosebleeds and bleeding from the gums and tongue are common and can occur without minor trauma or injury (spontaneous bleeding). Some people bleed between their joints and into their muscles. Rarely, bleeding into the brain or other internal organs can be fatal. Women with congenital afibrinogenemia may have abnormally heavy menstrual bleeding (menorrhagia). Without proper treatment, women with this condition may have difficulty getting pregnant and have repeated miscarriages.

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Introduction:-

Afibrinogenemia and Hypofibrinogenemia:

Afibrinogenemia and hypofibrinogenemia (fibrinogen deficiency type I) is a rare congenital disorder characterized by unmeasurable or low plasma levels of fibrinogen. Their genetic basis is represented by mutations in one of the three fibrinogen genes located on chromosome 4, FGA, FGB, and FGG (Casini, 2014). In afibrinogenemia, a rare autosomal recessive disorder, complete lack of detectable fibrinogen commonly leads to cord bleeding (Obeagu et al., 2022; Obeagu et al., 2022) . Other complications include intracranial bleeding after minor trauma, severe epistaxis, gum and gastrointestinal bleeding, ecchymosis, and spontaneous rupture of the spleen. Affected women may experience menorrhagia, recurrent miscarriages, and postpartum haemorrhage (Neerman-Arbez, 1999).

Congenital afibrinogenaemia, a rare disorder with an estimated incidence of 1-2 per million, is inherited in an autosomal recessive manner and the gene is located on chromosome 4. It is characterized by almost no fibrinogen due to impaired hepatocyte synthesis. Symptoms range from minimal to life-threatening bleeding and are common in the neonatal period and include hematoma or intracranial bleeding from birth trauma, umbilical bleeding, and excessive bleeding after circumcision. Similar to haemophilia, spontaneous bleeding, post-traumatic and post-operative excessive bleeding can be observed, leading to excessive ecchymosis, joint bleeding, gastrointestinal bleeding, and intracranial bleeding (Weisel, 2005). . In addition, menstrual bleeding can be heavy, and spontaneous abortions in early pregnancy are common. Laboratory screening tests using thrombus formation as an endpoint, including thrombin time, PT, and PTT, are greatly extended. A definitive diagnosis is made by measuring plasma fibrinogen, which is undetectable by both functional and immunological assays. Treatment consists of prophylactic or as-needed administration of plasma-derived fibrinogen concentrate, cryoprecipitate, or fresh frozen plasma, with concentrates being the therapeutic agent of choice. Afibrinogenaemia is a genetic condition caused by one or more genes not working properly. Disease-causing variants in the following genes are known to cause this disease:

FGA, FGB, FGG. A genetic variant is a change in the coding or DNA sequence of a gene that makes it different from most people. A benign variant does not affect the function of the gene and therefore does not cause health problems or disease. Pathogenic mutations cause health problems and diseases because they affect how genes work. Pathogenic variants are sometimes called mutations or disease-causing variants.

Afibrinogenaemia

Congenital afibrinogenaemia is caused by a complete deficiency of the fibrinogen protein. Most FGA, FGB, and FGG gene mutations that cause this condition provide premature stop signals to the instructions for making that particular protein. Even if a protein is made, it doesn't work. If a subunit is missing, the fibrinogen protein will not assemble and fibrin will not exist. As a result, blood clots fail to form in response to injury, leading to excessive bleeding seen in individuals with congenital afibrinogenaemia (de Moerloose, 2013).

Congenital afibrinogenaemia is inherited in an autosomal recessive manner. That is, there are mutations in both copies of the gene in each cell. Each parent of a patient with an autosomal recessive disorder has one copy of the mutated gene. Parents have blood fibrinogen levels that are about half normal, but do not usually have signs or symptoms of the disease (Williams, 2003).

Congenital hypofibrinogenaemia is a rare autosomal dominant disorder characterized by bleeding and obstetric problems such as abortion, postpartum hemorrhage, and recurrent miscarriage. This condition is defined as the presence of structurally normal fibrinogen at levels below 150 mg/dL. Mid-pregnancy miscarriages are believed to be caused by marginal bleeding. This is supported by data from fibrinogen-deficient transgenic mice that consistently experience abortions on day 10 (Weisel, 2005). Abortion in these mice is corrected by the addition of fibrinogen. Fibrinogenaemia is weakly associated with hypercoagulability rather than hypocoagulability.

A woman with hypofibrinogenaemia has reported a successful pregnancy using fresh frozen plasma or cryoprecipitate to maintain her fibrinogen level above 100–150 mg/dL. Each unit of cryoprecipitate contains approximately 300 mg of fibrinogen, increasing plasma concentrations by approximately 6 mg/dL. Thrombotic complications may be observed in afibrinogenic patients during replacement therapy with: B. Ischemic foot disease, ischemic stroke, renal or ovarian vein thrombosis, deep vein thrombosis and pulmonary embolism (Kobayashi, 2003). Thrombotic disorders such as protein C deficiency may be accompanied by afibrinogenaemia with susceptibility to thrombosis exacerbated by replacement therapy. Primary prevention with fibrinogen concentrate or cryoprecipitate should be considered at a young age to prevent bleeding.

Conclusion:-

Afibrinogenaemia is a very rare blood clotting disorder characterized by dysfunction or complete absence of plasma fibrinogen. Fibrinogen plays an important role in the final step of the clotting pathway. It is the basic molecule required for the formation of insoluble fibrin clots. Fibrinogen also acts as a bridge between platelets to form platelet clumps. The most common signs of afibrinogenaemia include cord bleeding and bleeding from mucosal surfaces, especially menorrhagia, epistaxis, and oral mucosal bleeding. Musculoskeletal bleeding accounts for half of patients, gastrointestinal and urinary bleeding in fewer. Replacement therapy with plasma-derived fibrinogen concentrate remains the main treatment for bleeding episodes. However, fresh frozen plasma, cryoprecipitate, and recombinant fibrinogen are being explored as alternative treatment options.

Fibrinogen Concentrate is available as replacement therapy for patients with afibrinogen. Cryoprecipitate and fresh frozen plasma (FFP) should be infused as an emergency only if fibrinogen concentrate is not available. Because fibrinogen concentrate was not available on the day of patient admission, FFP infusion was performed, resulting in controlled bleeding without treatment complications.

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