© IJHG 2020 Int J Hum Genet, 20(3): 120-131 (2020)
PRINT: ISSN 0972-3757 ONLINE: ISSN 2456-6330 DOI: 10.31901/24566330.2020/20.03.758

Thrombocytopenia and Lung Disorder - Interconnected? - An Overview

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KEYWORDS Biomarkers. *CFTR*. *F5gene*.Lung Disorder. *Platelet Endothelial Aggregation Receptor-1*. Thrombocytes

ABSTRACT Thrombocytopenia is a condition with thrombocyte count less than 1,50,000/µl of blood. As the conversion of proplatelets to thrombocytes occurs in the lung, it is also involved in the thrombocyte hemostasis.Therefore, the abnormal hemostasis of thrombocyte could affect the normal function of the lung as in the cases of cystic fibrosis, idiopathic pulmonary fibrosis, chronic obstructive pulmonary disorder, pulmonary thromboembolism and acquired respiratory distress syndrome. The present review interprets the possible connection between the thrombocytopenia and lung disorder with the help of biomarkers like anti-glycoprotein IIb/IIIa, plasma thrombopoietin, P-selectin, sCD40L, tumor necrosis factor α, serotonin and LTB_4 that are membrane glycoprotein, production factor, activation, aggregation, co-stimulatory product, chemical present in the thrombocytesandmolecular marker for lung disorder respectively. Genetic mutation in *F5gene*, *CFTR* and *PEAR1* thatwere found in factor *V* Leiden thrombophilia, cystic fibrosis and pulmonary thromboembolism interconnecting between the lung and thrombocytes are also discussed

INTRODUCTION

In thrombocytopenia, the thrombocyte count is below 2.5th of the normal value 1,50,000/µl (Manasa et al. 2016). The reduction in the thrombocytes are due to three main reasons like i) decrease in making of the thrombocyte ii) increase in the destruction of thrombocyte iii) changes in the distribution of thrombocyte (Zucker-Franklin and Philipp 2000). The fragmentation of megakaryocytes in the capillary isresponsible for releasing the thrombocytes in circulation (Johnson et al. 2010). It has been observed that the megakaryocytes in the lungs also produce thrombocytes, which gives importance tothe lung on thrombocyte homeostasis (Zucker-Franklin and Philipp 2000). Certain lung disorders like pulmonary thromboembolism, cystic fibrosis, chronic obstructive pulmonary disorder (COPD), acquired respiratory distress syndrome and idiopathic pulmonary fibrosis are found to have connections with thrombocyte malfunctioning (Tabuchi and Kuebler 2008). It has also been found that thrombocytes play various roles like interacting directly with the infectious bacteria, connecting with immune and endothelial cells while releasing immune mediators and even the toxins released by the bacteria alters the thrombocyte function in case of infectious and allergic lung diseases (Gomez-Casado et al. 2019). In a study with stable COPD, the thrombocytes count had a U shaped link with the maximum risk of 3-year all cause mortality (Fawzy et al. 2019).

The link between the thrombocytes and the lung can be efficiently understood with the help of biomarkers like P- selectin (Li et al. 2017), Thrombopoietin (Durk et al. 2013), anti-glycoprotein IIb/IIIa (Hoffmann 2014) associated with thrombocytes and LTB_4 (Kacerova et al. 2018) and sCD40L (Konstan et al. 2014) with lungs and also the biomarkers like serotonin. Thromboxane and tumor necrosis factor alpha which have interconnection between lungs and thrombocytes. The genetic association between these two are also known through *F5gene* (Croft et al. 2012), *CFTR* (Rafeeq and Murad 2017) and *PEAR1* (Li et al. 2017) genes.

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Objectives

The present review is aimed at identifying the interlink between the thrombocytopenia and lung disorders, the available biomarkers and the possible genetic mutations involved in association with lung and thrombocytes.

METHODOLOGY

This review is based on the data collected from PubMed search, PubMed Central, Science Direct and through google surfing. There were about 60 papers from PubMed, 30 papers from the PubMed Central and 10 papers from Science Direct platforms and more than 70 articles related were selected based on the keywords found in the title and abstracts. The keywords used to scrutinizing are thrombocytopenia, lung disorders, biomarkers for thrombocytopenia, association between the thrombocytopenia and lung disorders, genetic mutation in thrombocytopenia and genetic mutation in lung disorders.

OBSERVATIONS AND DISCUSSION

Thrombocytes and Thrombocytopenia

The small enucleate cell fragments present in the blood are called thrombocytes or platelets, they play a major role in the maintenance of vascular integrity and regulating hemostasis (Ghoshal and Bhattacharyya 2014). There are nearly 150,000-450,000/µl thrombocyte in the circulation of peripheral blood (Erkurta et al. 2012).The thrombocytes are responsible for the blood clotting as they have clotting protein fibrinogen. It is an important inflammatory marker (Cerletti et al. 2012). Some thrombocyte agonists stimulate the action of thrombocyte adhesion to sub endothelial surfaces during which the thrombocyte changes its shape, liberates its granule contents and thereby forms aggregates by adhering to each other (Vinik et al. 2001). The thrombocytes are said to be the structure that is capable of cellular functions excluding those that immediately dependent on the nucleus because they contain certain cytoplasmic organelles like mitochondria, components of the Golgi apparatus, endoplasmic reticulum and ribosomes (Han and Baker 1964). They have a life span of about 7-9 days(Tabuchi and Kuebler 2008).

Almost 75 percent of thrombocyte auto-antigens are located to either the thrombocyte *Glycoprotein*IIb/IIIa (GPIIb/IIIa) or *Glycoprotein*Ib/IX (GPIb/IX) complex (Yu et al. 2015). The auto reactive B cell produces auto-antibodies against the self-antigens like the immunoglobulin G (IgG) that produces antibodies to the GPIb/IIIa and/or GPIb/IX that is found to have a great importance in the thrombocyte destruction (McMillan 2000). There is a possibility that thrombocyte levels in the circulation can be decreased due to entry into a splenic pool (Aster et al. 1996). Thrombopoiesis the process by which the thrombocytes are produced and is influenced by the changes in the megakaryocytes number and its volume. The endomitosis changes of volume in megakaryocytes were found to be more relative to the thrombocyte count and it is a good indicator to find the thrombopoietic stimulus (Harker et al. 1969).

One of the most common blood disorder-called thrombocytopenia is a condition where there is an abnormally low number of thrombocytes due to various reasons (Izak and Bussel 2014). Thrombocytopenia is the result of a fall in thrombocyte count from 150,000/µl. Another cause of the low level of thrombocyte counts is the usage of medicines like, aspirin and heparin that are associated with interfering in either the function of thrombocyte or coagulation in a constantly growing population of the patients with cardiovascular and thromboembolic disorders (Zucker-Franklin and Philipp 2000). The most common reasons for the increased thrombocyte destruction are hypersplenism, dengue fever, Gaucher's disease and Zika virus (Rodak et al. 2012).Thrombocytopenia is found in patients with liver diseases and the mechanism is predicted to be caused by decreased production of thrombopoietin that has a major role in platelet production (Sanjo et al. 2003). Some medicines like valproic acid, methotrexate, H_2 blockers and proton pump inhibitors by the direct myelo suppression are associated with its causes (Houghton and Gray 2010).

Thrombocytopenia is the preliminary sign of various diseases like hematologic malignancies, infectious diseases, thrombotic microangiopathies, autoimmune disorders and is a common

symptom of certain medications (Izak and Bussel 2014). In chronic liver diseases the level of thrombocyte associated IgG and the volume of the spleen are noted, which implies that the immune mediated process and hypersplenism are important thrombocytopenic events (Sanjo et al. 2003). The symptom of this disease includes bruising, purpura, petechiaein legs and mucus membrane, which may be due to spontaneous bleeding under the skin (Houghton and Gray 2010). Thrombocytopenia is the second most occurring hematological disorder during the gestational period (Sullivan and Martin 1995). Thrombocytopenia can be classified based on the causes, which can be due to a decrease in thrombocyte production, increased thrombocyte depletion or due to any splenic damage (Smock and Perkins 2014).

Occurrence of Thrombocytopenia

Every 2 to 4/100,000 adults have immune thrombocytopenia, which might lead to viable bleeding symptoms (Lambert and Gernsheime 2017). In the adult patients who experience thrombocytopenia for the first time, the treatment is given with the aim to obtain a safe thrombocyte level in order to prevent bleeding and to extend their lifetime with minimal treatment related toxicity (Rodeghiero et al. 2009). The primary idiopathic thrombocytopenic purpura (ITP) occurs in about 3.3/100,000 adults per year while holding the prevalence of about 9.5/100,000 adults per year, the females are more likely to primary ITP in adults but in the elderly stage, both men and women are equally affected (Lambert and Gernsheime 2017). The gestational thrombocytopenia occurs in nearly 5 percent to 10 percent of women, which may develop during the pregnancy or immediately after the postpartum period (Cines and Levine 2018). The thrombocyte count below 20,000/µl to 30,000/µl indicates the risk of bleeding for a vaginal delivery (Webert et al. 2003), and thrombocyte count less than 50,000/µl is a risk for a cesarean section (Fujimura et al. 2002).An approximate of 50 million to 200 million people are affected by dengue fever globally, which has thrombocytopenia as an important clinical manifestation (Murray et al. 2013).

Lung Disorders

The lung disorder is a condition that is caused by an abnormality in the lungs that interferes with the airway damages. Lung disorders like cystic fibrosis, idiopathic pulmonary fibrosis, COPD, pulmonary thromboembolism and acquired respiratory distress syndrome are discussed in this review. Cystic fibrosis is a condition where there is a blockage in the lung due to thick mucus and neutrophil infiltration which leads to tissue degradation (Rafeeq and Murad 2017).The mutation in the Cystic fibrosis transcription receptor (CFTR) gene causes an alteration in the function of CFTR protein, which helps in conducting the chloride to pass through the mucus airway and then will be followed by water that makes the mucus thin if *CFTR* function is unaltered (Cystic Fibrosis Foundation 2016). The infiltration of neutrophils leads to the production of elastase that stimulates the lung antiproteases to degrade lung tissues and also produces a large amount of nucleic acids and cytosol matrix proteins resulting in hyperviscosity of mucus (Griese et al. 2008).

The idiopathic pulmonary fibrosis is due to an abnormally activated alveolar epithelial cells producing substances that mediate the formation of fibroblast and myofibroblast foci (King et al. 2011). COPD is characterized by the abnormal inflammatory response of the lungs to the gases or poisonous particles (McDonald 2005). One of the important venous thromboembolism is called the pulmonary thromboembolism where there is an obstruction in the airways of the lungs (Mabrouk et al. 2014). The acute respiratory distress syndrome is characterized by intense lung inflammation (Alhazzani et al. 2013).

Occurrence of Lung Disorder

Cystic fibrosis is found in about 100,000 people worldwide (Klimova et al. 2017). It is found in common among the white people of North European ancestry where 1 in every 2000-3000 have cystic fibrosis (Cystic Fibrosis Foundation 2014). Over three million people approximately are affected by idiopathic pulmonary fibrosis (Martinez et al. 2017). More than 200 million people in the world are affected by COPD, which will be the third leading disease by the year 2020

(Gao et al. 2015). There are about 2.68 cases of pulmonary thromboembolism in every 10,000 general thoracic surgeries (Yan et al. 2017). In the United States, there are about approximately 1,40,000 people affected by acute respiratory distress syndrome per year (Rubenfeld et al. 2005).

Interconnection between Lung Disorder and Thrombocytopenia

During the lung damage there is thrombocyte activation, aggregation and thrombi formation at the site of damage, which might lead to allow thrombocyte count in the circulation (Li et al. 2017). The fragmentation of megakaryocytes occurs in the blood capillaries of the lung and releases thrombocytes in the circulation (Zucker-Franklin and Philipp 2000). The thrombocytes were found to be in larger numbers in the pulmonary vein than in the pulmonary artery, which indicated that the lung may be responsible for thrombocyte production (Yang et al. 2015). The thrombocytes and thrombocyte endothelial interactions contribute to various lung diseases like COPD or idiopathic pulmonary fibrosis (Yang et al. 2003). Thrombocytopenia is found in acute respiratory distress syndrome mortality (Shan et al. 2011). In cystic fibrosis, the thrombocytes facilitate the recruitment of polymorphonuclear neutrophil granulocytes in the lung and also release their pro-inflammatory and anti-inflammatory agents (O'Sullivan and Kerrigan 2015). Alterations in the thrombocyte functions and numbers occur in systemic infectious syndromes that may include the lung and pleura, also including bacterial sepsis, malaria and dengue (Tabuchi and Kuebler 2008). The thrombocytes have the inflammatory activities, which in order helps in the defense of the lung, but it is also a reason for lung damage in the case of acquired lung infection or acquired respiratory distress syndrome (Bozza et al. 2009; Zarbock and Ley 2009; Weyrich and Zimmerman 2013; Earnest and Deane 2014; Vieira-de-Abreu et al. 2015). The thrombocytes have various important roles in maintaining the endothelial barrier function in the pulmonary circulation, one among which is the secretion of soluble molecules for the endothelial barrier function (Fontana et al. 2007).

Spingosine-1-phosphate is one of the soluble molecules released by the thrombocyte, which is required in stabilizing the pulmonary endothelium by enhancing the tight junctions and adherence junctions (Sullivan and Kerrigan 2015).The pulmonary thromboembolism occurs usually when there is a pathological condition of haemostasis, coagulation, and anticoagulation disorders, the thrombocytes are responsible for these functions and thrombocytes also play an important role in the thrombosis (Crisafulli et al. 2012). The incidence of interstitial lung disease has found to be developing in the acute phase of severe thrombocytopenia (Sharma et al. 2012). On the other side, there is an increase in circulating thrombocytes in the case of COPD (Francisca et al. 2012). In asthma patients the thrombocytes may transmigrate into the tissue and worsen allergic inflammation by releasing proinflammatory mediators in abundance, which may lead to non-eosinophilic airway inflammation(Sullivan and Kerrigan 2015). In COPD the thrombocytes are activated, and adherence occurs as like the case of asthma and cystic fibrosis, which stimulated more by cigarette smoking (Samanta and Sharma 2015).

Biomarkers and Diagnostics

The thrombocyte counts are the preliminary marker for detection of the thrombocytopenia. In the case of thrombocytopenia, which is due to dengue haemorrhagic fever there was an elevation in the serum alanine transaminases and aspartate transaminases level (Schwartz 2007). This condition is due to the reason that hepatocytes and Kupfer cells are the main targets for dengue virus infection (Semple and Freedman 1991). The anti-GPIIb/IIIa is the thrombocyte membrane glycoproteins for which the autoantibodies are produced in the idiopathic thrombocytopenic purpura by the abnormal T helper cells. Therefore, the levels of anti-GPIIb/IIIa are observed in idiopathic thrombocytopenic purpura (Hoffmann 2014; Porcelijn et al. 1998).

The immature thrombocytes are called as reticulated thrombocytes are one of the representing factors of megakaryopoiesis in the bone marrow, which can be helpful in diagnosing the various types of thrombocytopenia (Duerschmied et al. 2013). Plasma thrombopoietin has

a significant role in thrombopoiesis and also can differentiate between the cause of thrombocytopenia, which is either less production of thrombocytes or due to increased distruction of thrombocytes (Durk et al. 2013). The P-selectin can be a marker for thrombocyte activation, which in combination with megakaryocytes and thrombocytes count can be a useful marker in detecting anassociation between the lung disorder and thrombocytopenia (Li et al. 2017). The transforming growth factor β1 is a cytokine thatis important in maintaining the immune response, in increasing the collagen production in fibroblasts which in turn play a role in platelet aggregation (Pihusch et al. 2005).

The Toll like receptors play an important role in defense of the host against any pathogen with the help of cytokines they produce (Yu et al. 2015). The ratio between the T helper1 and T helper 2 is not normal in the case of autoimmune disorder.The notch signalling is important in the mekaryopoiesis of haematopoietic stem cells, which indeed has control over the platelet production (Ji et al. 2014). The glycoprotein Ib/IX/V is a complex that together forms the von Willebrand factor of the platelet surface receptor which is also affected during the thrombocytopenia (Millan et al. 2000). The lung disorder is diagnosed with the serial chest X-rays or computerized axial tomography scans to identify the lung infection by its morphology. The surfactant proteins SPA and SPD are important in maintaining alveolar epithelial stress and so their quantitative and qualitative variation depicts the lung disease (Ley et al. 2014).

The *KLC6/MUC1* expression has been found on type II Alveolar epithelial cell extracellular surfaces which will inturn represent wellness of the lung (Ishikawa et al. 2012). The small antimicrobial proteins called α-defensins levelwas found to be elevated in the case of acute exacerbation of idiopathic pulmonary fibrosis (Konishi et al. 2009). The cytokeratin 18 is a cytoskeletal protein found in an alveolar epithelial tissue, which was evident in the immunohistochemistry of an Idiopathic pulmonary fibrosis lung and not in the normal lung (Cha et al. 2012). A chemokine protein called CCL-18 is produced by alveolar macrophages and its responsibility includes stimulating the production of collagen in pulmonary fibroblasts (Kodera et al. 2005).

There is a dysfunction of YKL 40 in the case of COPD, asthma and in various acute and chronic inflammatory diseases because they are involved in tissue response to injury (Lee et al. 2011). The HSP 70 is expressed by the platelets itself and hence the anti- HSP 70 will help in determining the platelet homeostasis (Rigg et al. 2018). The lymphocyte aggregates in the lungs and had the expression of CXCL13 hence its variation is measured in the lung diseases (Vuga et al. 2014). MMP1 and MMP7are expressed by type II alveolar epithelial cells and where MMP1 plays a role in the degradation of type 1 and 3 collagen and the MMP7 is correlated with impairment in pulmonary function (Rosas et al. 2008). MMP1 and MMP7 are used as potent peripheral blood biomarkers in idiopathic pulmonary fibrosis (Pardo et al. 2005).The Periostin is an intracellular protein that aids in the closure of wounds, and blocking it would minimise the collagen deposit in the lung (Kudo 2011). The variation in CD4+ is observed in chronic adaptive immune activation (Gilani et al. 2010). The T-cells and Tregs are cells thatare the predominant markers of lung injury as they play an important role in immune modulation and activation. Circulating fibrocytes contribute to the pulmonary fibroblasts hence their variations are also to be noted in lung diseases (Tanjore et al. 2009). The Cys-LTs, LTB_4, 8-isoprostane, serotonin are molecular biomarkers for lung diseases which are mostly watched in asthma cases (Kacerova et al. 2018).

In the case of interstitial lung disorder and immune thrombocytopenia while the thrombocytopenic condition was diagnosed using the measurement of antibodies that are specific to thrombocyte glycoprotein by platelet associated IgG characterization assay and by platelet associated immunoglobulins (Fontana et al. 2007). There have been increased levels of serotonin in allergic inflammation of the human lungs when diagnosed with their segmental lavage fluid, which is due to the fact that most of the peripheral serotonin is present in the thrombocytes which would induce the accumulation of neutrophils to the site of inflammation and therefore the serotonin may be a target of therapy in the future to cure asthma (Davi et al. 1995).

In case of cystic fibrosis the urinary thromboxane level is found to be increased, which is a marker of thrombocyte activation (Bustamante et al. 2016). The rise in the level of a soluble costimulatory product of thrombocyte is sCD40L

(Konstan et al. 2014). Leukotriene B_4 is produced by the macrophages and the polymorphonuclear neutrophils as a response to the inflammation, which, along with interleukin-8 promotes accumulation of neutrophils in the airways (Berger 2002; Cockx et al. 2018). There is an accumulation of monocytes and macrophages at the site of inflammation in the lungs atcystic fibrosis (Kreisel et al. 2010). These monocytes are responsible for the production of cytokines that helps in neutrophil migration and activation, which indeed results in an elevated tumor necrosis factor-α that was observed in cystic fibrosis (Carpagnano et al. 2003). The overall list of diagnosing methods for a lung disorder and thrombocytopenia is listed in Table 1.

Table 1: The Biomarkers and diagnostic methods for both thrombocytopenia and lung disorder

Disease	*Biomarkers and diagnostics*
Thrombocytopenia	*Blood Proteins*
	P-selectin (Li et al. 2017)
	Plasma thrombopoietin (Durk et al. 2013)
	glycoprotein IIb/IIIa (Hoffmann 2014; Porcelijn et al. 1998)
	Serum alanine transaminases (Schwartz 2007)
	Serum aspartate transaminases (Schwartz 2007)
	Notch signalling (Ji et al. 2014)
	glycoprotein Ib/IX/V (Millan et al. 2000)
	von Willebrand Factor (Mercher et al. 2008; Millan et al. 2000)
	Blood Cells
	Transforming growth factor-²1-cytokine of Treg (Pihusch et al. 2005)
	Toll like receptor r (Yu et al. 2015)
	T helper 1 (Yu et al. 2015)
	T helper 2 (Yu et al. 2015)
	Reticulated thrombocytes (Duerschmied et al. 2013)
Lung Disorder	*Blood Proteins*
	Surfactant protein A (Ley et al. 2014)
	Surfactant protein D (Ley et al. 2014)
	Krebs von den Lungen-6 /mucin 1- KL6/MUC1 (Ishikawa et al. 2012)
	α- defensins (Konishi et al. 2009)
	cleaved cytokeratin 18- cCk 18 (Cha et al. 2012)
	CCL 18 (Kodera et al. 2005)
	YKL40 (Lee et al. 2011)
	Anti-HSP70 IgG [Heat shock protein 70] (Lee et al. 2011)
	C-X-C motif chemokine 13[CXCL13] (Vuga et al. 2014)
	MMP7 (Rosas et al. 2008; Pardo et al. 2005)
	MMP1 (Rosas et al. 2008; Pardo et al. 2005)
	Periostin (Kudo 2011)
	$CD4^+$ (Gilani et al. 2010)
	Exhaled Breath Condensate
	Cys-LTs (Kacerova et al. 2018)
	Leukotriene B4 (Kacerova et al. 2018)
	8-isoprostane (Kacerova et al. 2018)
	Seratonin (Kacerova et al. 2018)
	Blood Cells
	T cells (Yu et al. 2015)
	T regulator (Yu et al. 2015)
	Fibrocytes (Yu et al. 2015)
	Instrumental Analysis of Lung Morphology
	Chest X-rays: Computerized axial tomography
Thrombocytopenia in Association with Lung Disorder	*Blood Proteins*
	Tumor necrosis factor alpha-± (Cha et al. 2012)
	Serotonin (Pihusch et al. 2005)
	Soluble cluster of differentiation 40 L (Mercher et al. 2008)
	Thromboxane (Ji et al. 2014)
	IgG characterization assay (Fontana et al. 2007)

Genes Predicted

F5 Gene

The *F5* gene mutation is the main reason for the factor *V* Leiden thrombophilia in which the *F5* gene synthesizes an activated protein C that controls the coagulation events, that on mutation does not function properly and results in the clot formation in the lung (Croft et al. 2012). The location of the gene is 1q24.2. This gene is responsible for the factor V, which is a multi-domain pro-cofactor (Duga et al. 2004). The factor V along with protein S in the activated protein C-mediated inactivation of activated factor VIII has anticoagulant activity (Shen and Dahlback1994).

CFTR Gene

The *CFTR* gene mutation is responsible for causing the cystic fibrosis in the lungs. The mutation in this gene will affect the chloride channel function, which is one of the reasons for thrombocyte abnormality (O'Sullivan et al. 2005). The *CFTR* alteration affects the cystic fibrosis transmembrane receptor that controls the maintenance of mucociliary clearance and viscosity of mucus (Terheggen-Lagro et al. 2005). The chromosomal location of this gene is 7q31.2.

PEAR 1 Gene

The platelet endothelial aggregation receptor 1(*PEAR-1*) is a transmembrane protein involved in the thrombocyte contact induced activation (Kline et al. 1965). The *PEAR-1* gets activated when it is phosphorylated on specific tyrosine receptors and it stimulates increased membrane expression on activated thrombocytes which inturn results in the coagulation of platelets inpulmonary thromboembolic patients (Li et al. 2017). The *PEAR-1* gene is located on chromosome 1 and its position is 1q23.1 (Faraday et al. 2011).

Mechanism

The role of each above-mentioned gene in affecting platelets and resulting in lung disorder is given in Figure 1,which depicts that, the *F5*

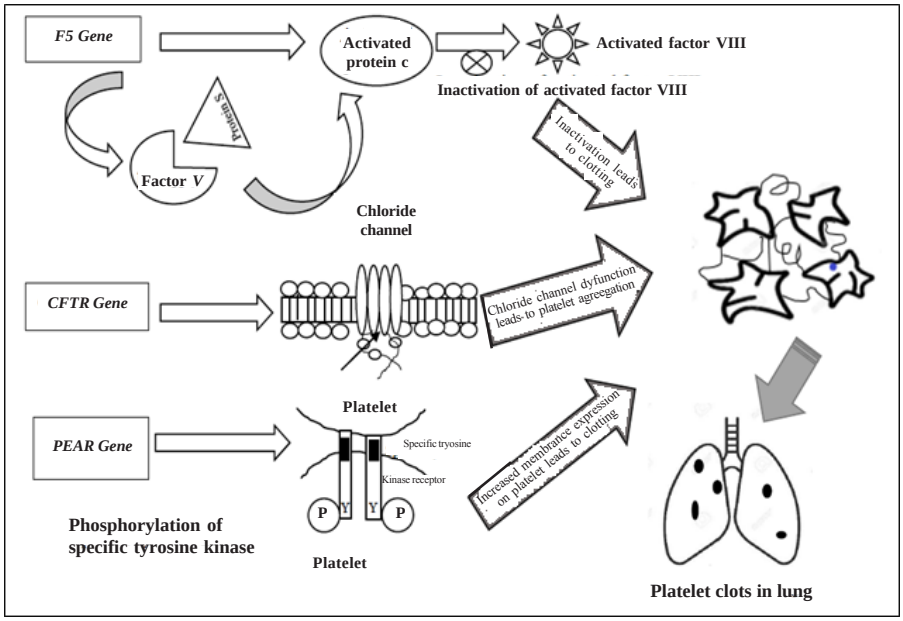

Fig. 1. The role of gene in affecting thrombocytes which may lead to lung disorder
Source: Authors

gene affects the activated protein C either directly or by affecting the factor *V* along with protein S. The activated protein C has control over the clotting mechanism of platelet which on the mutation of *F5 gene* may work abnormally and cause a clot in the lung as in case of factor V Leiden Thrompbhophilia. The *CFTR* gene influences the chloride channel function that is essential for the thrombocyte, this might affect the normal functioning and contribute to the clotting of platelets in the lung as in cystic fibrosis. The *PEAR1* gene by regulating on phosphorylation with specific tyrosine receptors, leads to the increased expression of themembrane of platelet in the case of mutation that on the other hand increases the clotting of thrombocytes as in the case of pulmonary thromboembolism.

Studies that Support Interconnection

In a study with cystic fibrosis patients, it was found that there was increased thrombocyte activation that leads to its aggregation and recommends thrombocyte activation as a prognostic element for cystic fibrosis (Lindberg et al. 2018). In COPD patients with thrombocytopenia, the all-cause mortality was found to be high (Fawzy et al. 2019).Thrombocytopenia was a marker for the mortality of patients with acute respiratory distress syndrome (Wang et al. 2014). In a case study, an elderly woman with thrombocytopenia was developing alveolar haemorrhage leaving out an suspicion of autoimmune patients developing non-infectious lung diseases (Hashmi et al. 2015). Thrombocytopenia was found to be severe in patients with severe refractory interstitial lung disease (Fontana et al. 2007). In a study, patients with idiopathic thrombocytopenic purpura were observed to develop the interstitial Pneumonia (Fontana et al. 2004).

The results above suggest that there are definite connection between certain lung disorders and the thrombocytopenia. The thrombocyte count can offer an efficientprognostic marker for lung disease development and worsening.

CONCLUSION

The thrombocytopenia is a disease that occurs most commonly in association with other diseases. The onset of thrombocytopenia either develops clinical symptoms of other diseases or the diseases that occurs in the organ of thrombocyte production that are indirectly involved in the pathogenesis of thrombocytopenia. The lung is found to be an organ involved in the production of thrombocytes. Hence, lung disorders and thrombocytopenia might be interlinked with each other which are probably found in the above lung disorders. There are also chances for genetic mutation underlying the association of these two diseases.

RECOMMENDATIONS

Therefore, further studies in the genes that are associated with the lung disorder and thrombocyte abnormality would lead a way to the prognosis of the diseases that would occur and to take the necessary action and also considering the observation of thrombocytes count in rest of the lung diseases and lung disorders would leave the importance of understanding thrombocytes which has numerous role in hemostasis of a human physiology.

ABBREVIATIONS

IgG - Immunoglobin G,
sCD40L- Soluble cluster of differentiation 40 L,
TNF-α -Tumor necrosis factor alpha,
CFTR - Cystic fibrosis transcription receptor,
PEAR 1 -Platelet endothelial aggregation receptor 1,
COPD - Chronic obstructive pulmonary disorder,
vWF- von Willebrand Factor,
Treg- T regulator,
SPA- Surfactant protein A,
SPD- Surfactant protein D,
sCD40L- Soluble cluster of differentiation 40 L,
Krebs von den Lungen-6 /mucin 1,
cCK18- cleaved cytokeratin 18, chemokine ligand 18,
HSP70- Heat shock protein 70,
CXCL 13- C-X-C motif chemokine 13,
CD- Cluster of Differentiation,
Cys- LTs- cysteinyl leukotrienes, and
LTB_4- Leukotriene B4.

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Paper received for publication in April, 2020
Paper accepted for publication in June, 2020