ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

The Significance of Pathophysiology Iron

Dr. Jyoti Batra[1], Dr. Juhi Aggarwal[2], Dr. Eram Hussian Pasha[3], Rana Sakshi Singh[4]

[1] Professor, Department of Biochemistry, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

[2] Professor & Head, Department of Biochemistry, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

[3] Assistant Professor, Department of Biochemistry, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

[4] MBBS Student, Batch 2021-22, Santosh Medical College and Hospital, Santosh Deemed to be University, Ghaziabad, Uttar Pradesh, India.

Email- [1] dean.research@santosh.ac.in, [2] jaggarwal38@gmail.com, [3] pasha.eram7@gmail.com, [4] ranasakshi2604@gmail.com

ABSTRACT:

Biological iron is needed but hazardous to organisms. This dual effect prompted numerous researchers to examine the mechanisms controlling its homeostasis in pathologic circumstances. The discovery of genes responsible for hereditary illnesses like hemochromatosis, the IRE/IRPs machinery, and the hepcidinferroportin axis has increased our understanding of iron metabolism. Deregulation of iron homeostasis, inflammation, and oxidative stress are often generated by iron buildup in pathologic situations. To provide a current state-of-the-art on the importance of iron in pathophysiologic conditions, we promoted a Research Topic with the contributions of top-leading scientists who studied the effects of iron homeostasis disruption on genetic, inflammatory, infectious, cardiovascular, and neurodegenerative diseases. This topic attracts some of the world's most eminent researchers, all of whom are dedicated to expanding our understanding of iron metabolism and its function in a wide range of human disorders.

Keywords: iron, iron metabolism, iron and genetic disorders, iron deficiency and anemia, iron and inflammation, iron and cardiotoxicity, iron and neurodegeneration, heme iron.

INTRODUCTION:

While biological iron is required for essential processes, too much of it can be harmful to the organisms that contain it. This dual impact piqued the curiosity of many researchers, who then set out to investigate the processes maintaining its homeostasis and how they are affected in a wide variety of pathologic situations. In recent times, the discovery of genes responsible for hereditary diseases, such as hemochromatosis, the IRE/IRPs machinery, and the hepcidinferroportin axis, dramatically increased our understanding of iron metabolism

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

and allowed us to unravel the basis of cellular and systemic iron homeostasis. In addition, these advancements revealed a causal connection between dysregulation of iron homeostasis, inflammation, and oxidative stress, which are frequently generated by the iron accumulation that is typically observed in a wide variety of pathologic diseases [1].

As a result of this, as we were of the opinion that it was time to provide an up-to-date state-of-the-art on the significance of iron in pathophysiologic conditions, we thought it would be a good idea to promote a Research Topic that would include the contributions of top-leading scientists who had researched the effects of iron homeostasis disruption on the outcome of genetic, inflammatory, infectious, cardiovascular, and neurodegenerative diseases. We were met with an interest that was even greater than our ambitions, and as a result, we were able to successfully collect 42 manuscripts that cover the major aspects of iron metabolism. These aspects range from the essential role that iron plays in the survival of cells to its contribution in the pathogenesis of a variety of diseases. They are now presented in an electronic book that is divided into 7 sections [2-5].

DISCUSSION:

There are 11 papers included in the first section of the Research Topic. These papers discuss the significance of iron in cellular proliferation, differentiation, and functioning, as well as its pivotal part in essential processes such as oxygen transport, DNA synthesis, metabolic energy, and cellular respiration. They describe the expression and regulation of the main players involved in the mechanisms of iron absorption, recycling, and mobilisation, the cooperation among different cellular compartments that facilitates iron mobilization/storage and prevents the deleterious effects induced by its accumulation, the role of iron in the Fenton chemistry as well as its effects on oxidative stress and programmed cell death, and the role of iron in the Fenton chemistry [6, 7]. Research into the many forms of circulating iron and the methods most frequently applied to its identification are topics that are of particular interest (Cabantchik, 2014). Additionally, the papers include up-to-date information regarding the iron metabolism of zebrafish and C [8]. elegans, as well as the role that iron plays in the skin and the regulatory systems that are dedicated to iron uptake, recycling, and mobilisation. When taken together, they provide the information necessary for a more in-depth comprehension of the role iron plays in the pathophysiology of diseases [9, 10].

In the second section, there are three studies that discuss the function of heme within cells as well as the cytotoxic effects of heme once it has been liberated from hemoproteins. In point of fact, the vast majority of iron in the body is found within the protoporphyrin ring, which serves as a prosthetic group in numerous hemoproteins that are necessary for the proper functioning of cells [11]. Reviewing the various aspects associated with heme synthesis, intracellular trafficking, scavenging, and catabolism, as well as the protective mechanisms that work together to prevent the deleterious effects induced by heme accumulation and the pathological conditions in which heme plays a dominant role, this article presents an

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

overview of these topics [12]. The expression and regulation of the primary heme scavengers and transporters that have been identified are also reviewed in this article (Korolnek and Hamza, 2014). Additionally, the concept that the maintenance of heme homeostasis is essential to prevent the deleterious effect induced by its overload is discussed in this article as well. In the following sections, we will discuss how a disruption in iron homeostasis is connected with a number of syndromes and how this association determines the results as well as the severity of these disorders [13].

Hemochromatosis, a genetic illness that is of essential importance for identifying the actors responsible for the control of iron in the system, is discussed in the third section of this chapter. It comprises two reviews on the genesis and genetic alterations that characterise this pathology, as well as the incidence, and several kinds of hemochromatosis that have been identified up until this point (Vujic, 2014). In "Silvestri et al., 2014," the authors detail not only the symptoms and manifestations that are typical of these disorders but also the changes that occur in the proteins that are accountable for them [14, 15].

The anaemia and iron deficiency issues that affect people all around the world are discussed in the fourth segment, which consists of four separate studies. The prevalence of iron deficiency in the general population, in particular throughout the ageing process, is analysed in this study [16]. We will discuss the causes of anaemia, including genetic diseases, inflammation, infections, bleeding owing to the development of ulcers, drug administration, and malignancies. In this study, Core et al. and Wang et al. evaluated the functions that TMPRSS6 and its substrate, hemojuvelin, play in the regulation of BMP signalling and hepcidin production [17, 18]. In conclusion, a summary is provided of the growing number of treatment options that target the many stages involved in hepcidin regulation, along with the encouraging results that were able to correct aberrant haematological parameters in animal models [19].

The connection between iron and inflammation, which is mostly mediated by the production of hepcidin, is the subject of the fifth section of this paper. This is one of the most current debates in the area. There are a total of seven papers featured. The first is an updated overview on the recognised struggle that takes place between the host and the pathogen for access to the iron that is required for growth, with specific reference to the extremely complicated malaria infection [12]. Infections caused by parasites, intracellular or extracellular pathogens are also discussed [14], along with the molecular pathways that contribute to disruption of iron homeostasis as a result of these infections. Important are both the impact of iron supplementation therapy on persons suffering from infectious diseases (Clark et al., 2014) and the involvement of proteins that restricting iron availability to bacteria may change the outcome of the infection. Both of these aspects are related to iron deficiency [20].

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

Six different publications are included in the discussion of the sixth segment, which is titled "The Role of Iron Overload in Cardiovascular Diseases." The first contribution is a review on the long-standing and opaque association between iron availability and anthracycline cardiotoxicity. The emphasis of this study is on the involvement of chelating agents and ferritins as agents guarding against the pro-oxidant activity of the drug [17]. In this article, a comprehensive description of the processes that contribute to the disruption of iron homeostasis and the impaired functioning of the heart is provided [15]. Iron's toxicity was studied in a variety of cell types, with a particular focus on the effects it had on macrophages in relation to the formation and progression of atherosclerotic plaque. In this section, a special emphasis is also given to the occurrence of cardiovascular problems and death in patients with hemochromatosis, which further confirms the role that iron plays in the aetiology of these diseases [13].

The last part of the book is the seventh section, which contains nine different studies and covers the role iron plays in neurodegenerative illnesses. Despite the fact that the regulation of iron homeostasis in the brain is still largely unknown, its disruption has been observed in a wide range of brain disorders, such as Parkinson's disease, Alzheimer's disease, Huntington's disease, Prion disease, and neurodegeneration with brain iron accumulation (NBIA).

This led to a plethora of studies being conducted to determine whether or not an excess of iron in the local environment is one of the causes of neuronal death (Wong and Duce, 2014). The pathogenic mechanisms that are connected with gene mutations of NBIAs that lead to neurodegeneration are reviewed, and it is shown that these mechanisms offer another close connection between iron dysregulation and oxidative damage (Levi and Finazzi, 2014), In addition, the role that inflammation plays in the development and progression of these pathologic disorders as well as its connection to the disruption of iron homeostasis was discussed in Urrutia et al(2014) .'s study (Urrutia et al., 2014). The positive effect of an oral iron chelator, the deferiprone, in scavenging excess iron from localised foci of siderosis is reviewed along with the ongoing clinical studies. This chelator is able to pass through the blood-brain barrier. According to Cabantchik et al. (2013), the chelator is said to have the ability to effectively move iron and to replenish regions that are deficient in iron. As a result, the symptoms of iron maldistribution are alleviated, and the harmful effects of iron overload are mitigated.

CONCLUSION:

In conclusion, this field of study attracts the participation of some of the most eminent researchers in the world, all of whom are dedicated to advancing our understanding of the significance of iron metabolism and the role it plays in a wide range of conditions affecting humans.

ISSN PRINT 2319 1775 Online 2320 7876

Research paper UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022

REFERENCES:

1. Basuli, D., Stevens, R. G., Torti, F. M., and Torti, S. V. (2014). Epidemiological associations between iron and cardiovascular disease and diabetes. Front. Pharmacol. 5:117. doi: 10.3389/fphar.2014.00117
2. Busti, F., Campostrini, N., Martinelli, N., and Girelli, D. (2014). Iron deficiency in the elderly population, revisited in the hepcidin era. Front. Pharmacol. 5:83. doi: 10.3389/fphar.2014.00083
3. Cabantchik, Z. I. (2014). Labile iron in cells and body fluids: physiology, pathology, and pharmacology. Front. Pharmacol. 5:45. doi: 10.3389/fphar.2014. 00045
4. Cabantchik, Z. I., Munnich, A., Youdim, M. B., and Devos, D. (2013). Regional siderosis: a new challenge for iron chelation therapy. Front. Pharmacol. 4:167. doi: 10.3389/fphar.2013.00167
5. Chiabrando, D., Vinchi, F., Fiorito, V., Mercurio, S., and Tolosano, E. (2014). Heme in pathophysiology: a matter of scavenging, metabolism and trafficking across cell membranes. Front. Pharmacol. 5:61. doi: 10.3389/fphar.2014. 00061
6. Clark, M. A., Goheen, M. M., and Cerami, C. (2014). Influence of host iron status on Plasmodium falciparum infection. Front. Pharmacol. 5:84. doi: 10.3389/fphar.2014.00084
7. Core, A. B., Canali, S., and Babitt, J. L. (2014). Hemojuvelin and bone morphogenetic protein (BMP) signaling in iron homeostasis. Front. Pharmacol. 5:104. doi: 10.3389/fphar.2014.00104
8. Gammella, E., Maccarinelli, F., Buratti, P., Recalcati, S., and Cairo, G. (2014). The role of iron in anthracycline cardiotoxicity. Front. Pharmacol. 5:25. doi: 10.3389/fphar.2014.00025
9. Korolnek, T., and Hamza, I. (2014). Like iron in the blood of the people: the requirement for heme trafficking in iron metabolism. Front. Pharmacol. 5:126. doi: 10.3389/fphar.2014.00126
10. Levi, S., and Finazzi, D. (2014). Neurodegeneration with brain iron accumulation: update on pathogenic mechanisms. Front. Pharmacol. 5:99. doi: 10.3389/fphar.2014.00099
11. Nairz, M., Haschka, D., Demetz, E., and Weiss, G. (2014). Iron at the interface of immunity and infection. Front. Pharmacol. 5:152. doi: 10.3389/fphar.2014.00152

ISSN PRINT 2319 1775 Online 2320 7876

Research paper **© 2012 IJFANS. All Rights Reserved, UGC CARE Listed (Group -I) Journal Volume 11, S Iss 4, 2022**

12. Penha-Goncalves, C., Gozzelino, R., and de Moraes, L. V. (2014). Iron overload in Plasmodium berghei-infected placenta as a pathogenesis mechanism of fetal death. Front. Pharmacol. 5:155. doi: 10.3389/fphar.2014. 00155

13. Poli, M., Asperti, M., Ruzzenenti, P., Regoni, M., and Arosio, P. (2014). Hepcidin antagonists for potential treatments of disorders with hepcidin excess. Front. Pharmacol. 5:86. doi: 10.3389/fphar.2014.00086

14. Silvestri, L., Nai, A., Pagani, A., and Camaschella, C. (2014). The extrahepatic role of TFR2 in iron homeostasis. Front. Pharmacol. 5:93. doi: 10.3389/fphar.2014.00093

15. Spottiswoode, N., Duffy, P. E., and Drakesmith, H. (2014). Iron, anemia and hepcidin in malaria. Front. Pharmacol. 5:125. doi: 10.3389/fphar.2014. 00125

16. Urrutia, P. J., Mena, N. P., and Nunez, M. T. (2014). The interplay between iron accumulation, mitochondrial dysfunction, and inflammation during the execution step of neurodegenerative disorders. Front. Pharmacol. 5:38. doi: 10.3389/fphar.2014.00038

17. Vinchi, F., Muckenthaler, M. U., Da Silva, M. C., Balla, G., Balla, J., and Jeney, V. (2014). Atherogenesis and iron: from epidemiology to cellular level. Front. Pharmacol. 5:94. doi: 10.3389/fphar.2014.00094

18. Vujic, M. (2014). Molecular basis of HFE-hemochromatosis. Front. Pharmacol. 5:42. doi: 10.3389/fphar.2014.00042

19. Wang, C. Y., Meynard, D., and Lin, H. Y. (2014). The role of TMPRSS6/matriptase2 in iron regulation and anemia. Front. Pharmacol. 5:114. doi: 10.3389/fphar.2014.00114

20. Wong, B. X., and Duce, J. A. (2014). The iron regulatory capability of the major protein participants in prevalent neurodegenerative disorders. Front. Pharmacol. 5:81. doi: 10.3389/fphar.2014.00081