Original Research Paper

Volume - 13 | Issue - 03 | March - 2023 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Biological Science

ASSOCIATION OF SERUM FERRITIN IN POST COVID-19 ANAEMIC PATIENTS TREATED WITH UMBILICAL CORD BLOOD AND HAEMATINICS.

Biplabendu Talukdar*	PhD scholar Department of Biochemistry & Biophysics, Kalyani University, Nadia. Assistant Professor, Department of IHBT, MCH, Kolkata. *Corresponding Author
Rita Ghosh	Professor, Department of Biochemistry & Biophysics, Kalyani University. Nadia
Niranjan Bhattacharya	Former Professor & Head Department of RMTS, STM, Kolkata , West Bengal.
Moinuddin Naskar	Senior obstetrician and gynaecologist, Vidyasagar hospital, Kolkata.
Priyadarshi Sengupta	PhD scholar , department of RMTS,STM,Kolkata

ABSTRACT COVID-19 patients commonly present with lower respiratory symptoms with other systemic involvement. Haematological manifestation such as low haemoglobin, thrombocytopenia, lymphocytopenia also common in COVID-19 patients. In this study, we investigated prevalence, association with serum ferritin in post COVID-19 anaemic patients, after human umbilical cord blood transfusion in relation to control group. Among 155 COVID-19 RT-PCR positive patients 36 (23%) was anaemic. In our study 18 patients was transfused human umbilical cord blood, 12 patients were treated with haematinics and 6 patients denied taking any of the above. In most cases anaemia was moderate to severe that may be due to inflammation or due to pre-existing iron deficiency.Umbilical cord blood transfusion to post COVID -19 patients for the treatment of anaemia because of the unique composition of UCB. Haematological analysis and serum ferritin estimation reflecting the treatment out come in post COVID-19 anaemic patients. There was a difference between the dependent variable's serum ferritin ($p < .001$) in anaemic COVID-19 patients. In conclusion, our result highlight serum ferritin is widely used in diagnosis and monitoring of COVID-19 disease.

KEYWORDS : COVID -19, RT-PCR, umbilical cord blood, serum ferritin

Introduction

The novel Corona virus disease 2019 (COVID-19) is a potential threat for civilisation. The disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Incubation period of SARS, COVID-19 is 1–14 days. SARS-CoV-2 commonly transmitted by either through aerosol or fomite [1]. Majority of patients were asymptomatic, and some patients present with symptoms of fever, cough, fatigue, breathing difficulties, anaemia, cytopenia and loss of taste and smell [2].

Some patients on post-acute infectious sequel of COVID-19 reports following symptoms of fatigue, dyspnoea, chest pain, patients are asymptomatic or having mild symptoms and eventually recover, some COVID-19 patients experiencing symptoms long after their COVID-19 polymerase chain reaction test (RT-PCR) turns negative; this is commonly referred to as "post-COVID-19 syndrome" or "long COVID." As per the National Institute for Health and Care Excellence (NICE), Post COVID-19 syndrome is defined as, "signs and symptoms that develop during or after an infection consistent with COVID-19, continuing for more than 12 weeks (3 months), and not explained by an alternative diagnosis." [3].

Pathophysiology of COVID

The lungs are the primary site of COVID-19 infection [4]. Human angiotensin-converting enzyme 2 (ACE2) is the major receptors for the entry of virus to the host cells. There are four main structural proteins: i) spike (S), ii) envelope (E) glycoprotein, iii) nucleocapsid (N), iv) membrane (M) protein. Other than four structural proteins, there are 16 non-structural and 5-8 accessory protein[5] .

Two subunit of spike protein S1 and S2 helps in binding of ACE2 receptors of the host cells and imitate virus through transmembrane serin protease 2 (TMPRSS2) [6]. ACE2 receptors not only present abundantly on type II alveolar respiratory epithelium, ACE2 receptors are also present other organs such as the upper oesophagus, enterocytes of the gastro-intestinal tract such as ilium, cardiomyocytes, urogenital tract like proximal tubular cells of the kidney, and urothelial cells of the bladder[7].

SARS-CoV-2 mediated pneumonia may occur in two phases, in the early phase there are direct virus replication induced tissue damage, followed by infected host cells trigger the immune response. Immune reaction due to infected host cells mobilizes T lymphocytes, monocytes, and neutrophils. Mobilization of neutrophils, monocytes released various cytokines such as, interleukin-1 (IL-1), interleukin-6 (IL-6),), IL-1β, IL-8, IL-12 tumour necrosis factor-α (TNF α), granulocyte-macrophage colony-stimulating factor (GM-CSF) and interferon (IFN)-γ. Occasionally circulatory high secretion of IL6 and TNF-α may results in a 'cytokine storm'[8,9].Inflammatory cytokines causes increase vascular permeability and ensuing of pulmonary oedema , inflammatory myocarditis, hepatic injury, GI mucosal injury etc. Peri-vascular inflammation may initiate microvascular microthrombi deposition and vascular injury followed by haematological changes [10,11,12]. Binding with Toll-Like receptors (TLR) also persuade the release of pro-IL-1β, which splits the active mature IL-1β until lung fibrosis occurs [13]. Inflammation intensely affects erythropoiesis through different mechanism, pro-inflammatory cytokines like interferon γ, IL-1,IL-33,TNF-α and interleukin-6 initiate abnormal iron metabolism [14].All the inflammatory mediators exerts inhibitory effects on erythroid progenitor and precursor cells that may reduce erythroid lifespan [15-19]. Inflammatory processes associated with COVID-19 may initiate anaemia due to iron deficiency. Serum ferritin is iron storage protein, a single ferritin molecule can sequester up to 4500 iron atoms. Circulatory low serum ferritin reflects low intracellular storage of irons [20]. Serum ferritin also reflect as a inflammatory markers due to release of serum ferritin from damage cells [21].

Human umbilical cord blood (HUCB) contains an average of 80-90 ml of blood at term. Which is rich in foetal haemoglobin (HbF) that has the potential to carry 60 percent more oxygen than adult haemoglobin (Hb [22]. HUCB also has a higher platelet concentration of 750000 against 250000 per micro litre of adult blood and a WBC count of 24,000 against 6500-10,500 cells/μL in adult blood. [23] HUCB has also been found to contain an array of anti-inflammatory cytokines like IL-10, IL-4 etc. [24].

Methods

The study was conducted at the Department of Regenerative Medicine and Translational Science, School of Tropical Medicine (STM) and Department of Biochemistry and Biophysics, Kalyani university after obtaining the ethical permission [CREC-STM/2020-AS-27 dated on 18/08/2020] from the institute. The study was conducted from July

2020 to December 2021.

Nearly 1500 COVID-19 RT-PCR reactive patients examined during July 2020 to December 2021 at different OPD or IPD, out of 155 patients were participates in our study among them 36 were anaemic. The criteria for selecting subjects for the study were 18-70 years old, both male and female volunteers, patients having haemoglobin levels less than equal to 10g/dL and post COVID patients voluntary participating in study. While the patients suffering from COVID-19 pneumonia & severe anaemic patients requiring urgent blood transfusion, not adhering to the study protocol, missing follow up visits, decision made by the expert clinical team. Anaemic patients due to unknown causes, haemoglobinopathies and systemic disease and patients having the presence of other chronic ailments e,g CKD, COPD, hypertension, malignancy were excluded from the study. The control group comprised of 12 Post Covid-19 patients with anaemia who had been treated with haematinics and other standard therapy as decided by the clinical expert team in the department. The experimental group consisted of 6 post Covid-19 patients with anaemia who had been transfused with freshly collected human umbilical cord blood (UCB). The study was conducted up-to 4 months from the day 0 or baseline study day.

Collection of umbilical cord blood and transfusion.

Human umbilical cord blood was collected from consenting mothers aseptically after lower uterine caesarean section (LUCS) under general or regional anaesthesia. In case of gross prematurity or dysmaturity, or if the projected weight of the foetus was less than 2 kg in USG, or if the mother suffered from any specific disease like hepatitis, HIV, etc., the cord blood collection was abandoned. Cord blood was collected only from informed, healthy mothers with their consent, after their healthy babies were born. The collection was started only after the baby was safely removed from the operation field, and the anaesthetist verified that the physical condition of the mother was stable. Decision to proceed with umbilical cord collection was taken by the obstetrician, only after that cord was immediately disinfected by spirit/Betadine solution. Umbilical cord blood was collected by puncture of the umbilical vein. A 16-g needle was attached umbilical cord blood collection bag. Blood bag contained 14 ml CPDA as anti-coagulant (citrate, phosphate dextrose adenine solution). Blood was collected as per flowed by gravity, and generally it was taken 3to 5 minute for 80-100 ml of the cord blood collection.

After collecting the cord blood in cord blood bag (Terumo penpolTM ,Mfg Date-06-05-2020 & Exp Date 05-05-2022), all units safely preserve at normal room temperature (20-240C) until the transfusion related infective markers was negative. All units were tested for HIV, HbsAg, antiHCV by ELISA (enzyme linked immune sorbent assay) by RPR (rapid plasma regain) for Syphilis & microscopical examination for malaria. All screening negative units were tested for ABO & Rh blood group. Volume and specific gravity were calculated by CompoScale CS300 (Terumo penpolTM). Peripheral smear was examined by using freshly prepared slides by gimsa stain for identifying morphology of different cells along with validate the test result by cell counter (Sysmex ,Erba, Transasia).

ABO group [using antisera of J.mitra,Tulip and Meri as per availability] matched available units were transfused in day care basis under supervision at their nearest hospital prior taken a consent of COVID-19 anaemic recipients, average 90 ml of cord blood transfused by blood transfusion set under supervision.

Parameters of laboratory investigation and follow up

All COVID-19 patients were followed up for consecutive 4 months, which had been conducted from Day 0 or baseline study day. Both control groups and experimental groups were assessed clinically along with other laboratory parameters. The patients were classified anaemic mild >9.5g/L, moderate anaemia < 9.5g/L to 8 g/L and sever if <8 g/L[..]. Iron deficiency anaemia diagnosed as per value of MCV, MCH value. Serum ferritin estimation during enrolment and end of follow of patients along with CBC reports helps in monitoring the COVID-19 patients. Low haemoglobin, MCV < 80fl, MCH < 26 pg, and serum ferritin < 30ng/ml suggestive anaemia; a serum ferritin > 100 with CBC features defined anaemia in chronic disease. Consecutively all COVID-19 patients were tested for Direct Coombs test, Indirect Coombs test and auto control using column agglutination card [Tulip diagnostic(P) Ltd, matrix gel system) along with complete blood count (Sysmex ,Erba, Transasia). for monitoring the transfusion related adverse events.

Collection of umbilical cord blood under local anaesthesia aseptically from operation theatre .

Statistical analysis:

Data were analysed by descriptive statistics and result reported as mean, median and SD, depending on each variable value distribution. Difference between groups were test by Kruskall-wallis test followed by Mann-Whitney's test, Bonferroni Post-hoc test. All tests were two-sided difference and correlation were considered significant if $p<0.05$.

All data are checked and analysed by online "DATAtab" calculator with analytical software Excel & IBM SPSS .20

Results:

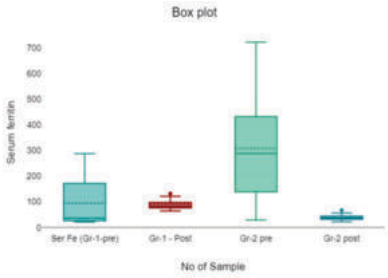
In table 1 laboratory parameters of the patients investigated in the present study. Comparing COVID-19 patients laboratory data characterized by lower Hb concentration and serum ferritin was analysed in different groups. In this study mean serum ferritin was higher in pre-transfused COVID-19 patients that is 307.76ng/ml than patients those were taking haematinics 93.63 ng/ml.

Table-1

	Ser Fe (Gr-1-pre)	Gr-1 - Post	Gr-2 pre	Gr-2 post
Mean	93.63	90.42	307.76	38.78
Std. Deviation	98.47	23.92	202.32	10.94
Minimum	21	64	29	22
Maximum	287	132	721	67

Gr-1 (COVID-19 patients with medication) serum ferritin pre/post treatment

Gr-2 (COVID-19 patients with cord blood transfusion pre /pos treatment.



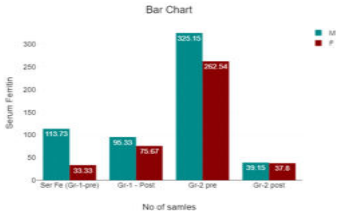
Box plot -fig -1

In table2, descriptive analysis pre medication and pre transfusion serum ferritin in COVID-19 male patients were 113.73 ng and 325.15 ng , in female patients 33.33 ng and 262.54 ng . In this study in table -3 pre-treatment MCV was 78.33 fl and 77.5 fl respectively, which signified as microcytosis (Normal MCV- 80-100 fl). Post medication follow up study serum ferritin was 95.33 pg and 75.67 in male and female participants whereas post transfusion serum ferritin was 39.15 fl and 37.8 among male and female participants.

Table-2 Descriptive analysis

		Sex (Gr-1)	
		M	F
	Frequency	13	5
Ser Fe (Gr-1-pre)	Mean	113.73	33.33
	Std. Deviation	107.2	9.24
	Minimum	21	28
	Maximum	287	44
Gr-1 - Post	Mean	95.33	75.67
	Std. Deviation	25.54	10.12

	Minimum	67	64
	Maximum	132	82
Gr-2 pre	Mean	325.15	262.54
	Std. Deviation	217.67	168.18
	Minimum	67	29
	Maximum	721	432
Gr-2 post	Mean	39.15	37.8
	Std. Deviation	12.44	6.53
	Fequency	13	5
	Minimumue	22	29
	Maximum	67	46



Bar chart -fig 2

Table -3

	MCV Gr-1	MCV-Gr2
Mean	78.33	77.5
Std. Deviation	3.57	4.63
Minimum	69	67
Maximum	82	85

Table- 4 statistical analysis

	Type III Sum of Squares	df	Mean Squares	F	p
Treatment	555,366.69	3	185,122.23	12.4	<.001
Within	1,047,968.25	36	29,110.23		
Error	492,601.56	33	14,927.32		

In table 4 There was a difference between the dependent variables of serum ferritin in different group $p < 0.001$ which significant.

Among 30 COVID-19 anemic patients, 20 were male and 10 were female. Mean base line pre transfusion hemoglobin was in male individual 7.77 gm/dl and female individual 8.09 gm/dl (table -3). Persons those were offered for hematinic (Ferus sulphate tablet as per dose), had mean base line Hb for male 7.81m/dl and female 8.07gm/ dl. Hemoglobin of all categories were measured after 24 hours and 1 month after the initial managements. Post transfusion Hb was male 8.16 gm/dl and female individual was 8.59 gm/dl and symptoms for anemia also relived. Whereas there were changes of Hemoglobin (Hb) were observed person having medication for anemia after 24 hours.

Discussion.

Serum ferritin is a iron storage protein, a single ferritin molecule can sequester up to 4500 iron atoms. Circulatory low serum ferritin reflects low intracellular storage of irons [25]. Serum ferritin also reflect as an inflammatory marker due to release of serum ferritin from damage cells [26]. In this study in spite low MCV <80 fl (normal MCV -80-100 fl), low haemoglobin serum ferritin increase > 100 fl. Here more serum ferritin signifies release of ferritin from damage cells due to COVID-19 mediated inflammatory reaction. All the inflammatory mediators exert inhibitory effects on erythroid progenitor and precursor cells that may reduce erythroid lifespan [27,28,29,30,31]. Inflammatory processes associated with COVID-19 may initiate anaemia due to iron deficiency.

Blood and blood products mainly used for correction of anaemia, thrombocytopenia, granulocytopenia, coagulation enzyme deficiency for correction diseases during emergency. All developed and developing countries mostly uses blood and blood components collected from voluntary non remunerated blood donors. Red blood cell alloimmunization and autoimmunization remain a major issue related blood transfusion [32]. Reliable supply of whole blood transfusion is a major issue in blood transfusion practice. Human umbilical cord blood transfusion is not a routine practice for correction of anaemia due to ethical related issues. Bhattacharya et all published a data in relation to cord blood transfusion and its safety efficacy [33]. In this study 18 COVID-19 anaemic patients were transfused compatible cord blood units for correction of anaemia, there was a significant change of haemoglobin in post 24 hours of cord blood transfusion. but with very little effects of serum ferritin in post cord blood transfusion, signifies inability to correct iron deficiency, whereas patients treated with medication recovered slowly, but correction of iron deficiency was more pronounced in medicinal treatment. Compare to medication and cord blood units' transfusion anaemic patients were symptomatically improved earlier. After following up none of them develop neither develop transfusion related allo or auto antibodies [34-35]. There were several advantages of cord blood transfusion is -i) Ease to procurement, processing, and storage. ii) there was minimum to no risk umbilical cord blood donors. iii) Reduce risk of cord blood transfusion related infection [36,37]. Iv) umbilical cord blood possess a smaller number of antigenic sites over the red cell membrane and HLA antigens in nucleated cells [38,39,40,41]. V) cord blood contain various immunomodulatory cells which is anti-inflammatory in nature.

Conclusion:

Serum ferritin has a dual role, which is a good indicator of iron deficiency anaemia and alternatively increase serum ferritin is a bio marker for acute inflammation.

Acknowledgements: Dr. Prasun Bhattacharya, Mr. Supriyo Roy, Mrs Sanchayita Talukdar, Ms. Seoti Talukdar, Dr. Swarnendu Dutta,Mr. Subhasish Chakraborty, Mr.Bratish Neogi.

REFERENCES:

1. Talukdar B;An overview of transmissibility and Severity of COVID-19; JMR2020;6(2): 46-47.
2. Suvvari TK, Simhachalam Kutikuppala LV, Babu GK, Jadhav M. Un- derstanding the unusual viral outbreak: coronavirus disease 2019. J Curr Res Sci Med. 2020;6:3[illegible]10. https://doi.org/10.4103/jcrsm.jcrsm_30_20.
3. Ani Nalbandian,Sehgal K, Gupta A; Post -acute COVID-19 syndrome; Nature Medicine 2021;vol 27 ;April.601-615.
4. Parasher Anant,COVID-19: Current understanding of its pathophysiology, clinical presentation and treatment : postgraduate med J 2021;97:312-320.doi10.1136/postgradmedj-2020-138577
5. Campbell DJ. Neprilysin Inhibitors and Bradykinin. Front Med (Lausanne) 2018;5:257. [PMC free article] [PubMed] [Google Scholar]
6. Mallela J, Yang J, Shariat-Madar Z. Prolylcarboxypeptidase: a cardioprotective enzyme. Int J Biochemist Cell Biol. 2009;41(3):477–481. [PubMed] [Google Scholar]
7. Ngo M-L, Mahdi F, Kolte D, Shariat-Madar Z. Upregulation of prolyl carboxypeptidase (PRCP) in lipopolysaccharide (LPS) treated endothelium promotes inflammation. J Inflamm. 2009;6(1):3. [PMC free article] [PubMed] [Google Scholar]
8. Han Y, Du J, Su H, Zhang J, Zhu G, Zhang S, et al. Identification of Diverse Bat Alphacoronaviruses and Betacoronaviruses in China Provides New Insights Into the Evolution and Origin of Coronavirus-Related Diseases. Front Microbiol. 2019;10:1900. [PMC free article] [PubMed] [Google Scholar]
9. Yuen K-S, Ye Z-W, Fung S-Y, Chan C-P, Jin D-Y. SARS-CoV-2 and COVID-19: The most important research questions. Cell Biosci. 2020;10(1):1–5. [PMC free article] [PubMed] [Google Scholar]
10. Zhang T, Wu Q, Zhang Z. Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. Curr Biol. 2020. [PMC free article] [PubMed].
11. Yuen K-S, Ye Z-W, Fung S-Y, Chan C-P, Jin D-Y. SARS-CoV-2 and COVID-19: The most important research questions. Cell Biosci. 2020;10(1):1–5. [PMC free article] [PubMed] [Google Scholar]
12. Zhang T, Wu Q, Zhang Z. Probable pangolin origin of SARS-CoV-2 associated with the COVID-19 outbreak. Curr Biol. 2020. [PMC free article] [PubMed]
13. Spiteri G, Fielding J, Diercke M, Campese C, Enouf V, Gaymard A, et al. First cases of coronavirus disease 2019 (COVID-19) in the WHO European Region, 24 January to 21 February 2020. Eurosurveillance. 2020;25(9):2000178. [PMCfree article] [PubMed] [Google Scholar].
14. Bergamaschi G, Borrelli de Andreis F, Aronico N, Lenti MV, Barteselli C, Merli S, Pellegrino I, Coppola L, Cremonte EM, Croce G, Mordà F, Lapia F, Ferrari S, Ballesio A, Parodi A, Calabretta F, Ferrari MG, Fumoso F, Gentile A, Melazzini F, Di Sabatino A; Internal Medicine Covid-19 Collaborators. Anemia in patients with Covid-19: pathogenesis and clinical significance. Clin Exp Med. 2021 May;21(2):239-246.
15. Orsini M, Chateauvieux S, Rhim J, et al. Sphingolipid-mediated inflammatory signaling leading to autophagy inhibition converts erythropoiesis to myelopoiesis in human hematopoietic stem/progenitor cells. Cell Death Differ. 2019;26:1796–1812. doi: 10.1038/s41418-018-0245-x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
16. Libregts SF, Gutiérrez L, de Bruin AM, et al. Chronic IFN-γ production in mice induces anemia by reducing erythrocyte life span and inhibiting erythropoiesis through an IRF-1/PU.1 axis. Blood. 2011;118:2578–88. doi: 10.1182/blood-2010-10-315218. [PubMed] [CrossRef] [Google Scholar]
17. Means RT, Jr, Dessypris EN, Krantz SB. Inhibition of human erythroid colony-forming units by interleukin-1 is mediated by gamma interferon. J Cell Physiol. 1992;150:59–64. doi: 10.1002/jcp.1041500109. [PubMed] [CrossRef] [Google Scholar]
18. Swann JW, Koneva LA, Regan-Komito D, Sansom SN, Powrie F, Griseri T. IL-33 promotes anemia during chronic inflammation by inhibiting differentiation of erythroid progenitors. J Exp Med. 2020;217:e20200164. doi: 10.1084/jem.20200164. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
19. Zoller EE, Lykens JE, Terrell CE, et al. Hemophagocytosis causes a consumptive anemia of inflammation. J Exp Med. 2011;208:1203–1214. doi: 10.1084/jem.20102538. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
20. Wang, W., Knovich, M. A., Coffman, L. G., Torti, F. M., & Torti, S. V. (2010). Serum ferritin: Past, present and future. Biochimica et Biophysica Acta (BBA) - General Subjects, 1800(8), 760-769. https://doi.org/10.1016/j.bbagen.2010.03.011
21. Kell DB, Pretorius E. Serum ferritin is an important inflammatory disease marker, as it is mainly a leakage product from damaged cells. Metallomics. 2014 Apr;6(4):748-73. doi: 10.1039/c3mt00347g. PMID: 24549403.

22. Usher R, Shephard M, Lind J. The blood volume of the new-born infants and the placental transfer. Acta Pediatr. 1963;52:497.
23. Bhattacharya N, Philip Stubblefield; Frontiers of Cord Blood Science 2009; springer , ,chapter 10,page no-230-231
24. Guyton AC, Hall JE. Textbook of Medical Physiology. Bangalore; WB Saunders. 1996:1036.
25. Bergamaschi, G., Aronico, N., Lenti, M. V., Barteselli, C., Merli, S., Pellegrino, I., Coppola, L., Cremonte, E. M., Croce, G., Mordà, F., Lapia, F., Ferrari, S., Ballesio, A., Parodi, A., Calabretta, F., Ferrari, M. G., Fumoso, F., Gentile, A., Melazzini, F.. Sabatino, A. D. (2021). Anemia in patients with Covid-19: Pathogenesis and clinical significance. Clinical and Experimental Medicine, 21(2), 239-246. https://doi.org/10.1007/s10238-020-00679-4
26. Datta S . et al ; Frequency of red cell alloimmunization and autoimmunization in thalassemia patients: a report from Eastern India;2015,Advances in hematology.
27. Bhattacharya N, Philip Stubblefield; Frontiers of Cord Blood Science 2009; springer , ,chapter 10,page no-xxii.
28. Talukder B et al; Safe red blood transfusion, a challenge in auto-immune hemolytic anemia patients;2016,GJTM 1(2):78.
29. Bhattacharya N, Philip Stubblefield; Frontiers of Cord Blood Science 2009; springer , ,chapter 10,page no-230-231.
30. Mommaas B, Steghuis-Kamp J, van Halteren AG, et al. Cord blood comprises antigen experienced T cells specific for maternal minor histocompatibility antigen HA-1. Blood. 2005;105:1823–1827.
31. Wagner JE, Barker JN, DeFor TE, et al. Transplantation of unrelated donor umbilical cord blood in 102 patients with malignant and non-malignant diseases: influence of CD34 cell dose and HLS disparity on treatment-related mortality and survival. Blood. 2002;100:1611–1618.
32. Rocha V, Wagner JE, Sobocinski KA, et al.; Eurocord and International Bone Marrow Transplant Registry Working Committee on Alternative Donor and Stem Cell Sources. Graftversus-host disease in children who have received a cord-blood or bone marrow transplant from an HLA identical sibling. N Engl J Med. 2000;342:1846–1854.
33. Michel G, Rocha V, Chevret S, et al.; the Eurocord Group. Unrelated cord blood transplantation for childhood acute myeloid leukaemia: a Eurocord Group analysis. Blood. 2003;102:4290–4297.
34. Orsini M, Chateauvieux S, Rhim J, et al. Sphingolipid-mediated inflammatory signaling leading to autophagy inhibition converts erythropoiesis to myelopoiesis in human hematopoietic stem/progenitor cells. Cell Death Differ. 2019;26:1796–1812. doi: 10.1038/s41418-018-0245-x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
36. Libregts SF, Gutiérrez L, de Bruin AM, et al. Chronic IFN-γ production in mice induces anemia by reducing erythrocyte life span and inhibiting erythropoiesis through an IRF-1/PU.1 axis. Blood. 2011;118:2578–88. doi: 10.1182/blood-2010-10-315218. [PubMed] [CrossRef] [Google Scholar]
37. Means RT, Jr, Dessypris EN, Krantz SB. Inhibition of human erythroid colony-forming units by interleukin-1 is mediated by gamma interferon. J Cell Physiol. 1992;150:59–64. doi: 10.1002/jcp.1041500109. [PubMed] [CrossRef] [Google Scholar]
38. Swann JW, Koneva LA, Regan-Komito D, Sansom SN, Powrie F, Griseri T. IL-33 promotes anemia during chronic inflammation by inhibiting differentiation of erythroid progenitors. J Exp Med. 2020;217:e20200164. doi: 10.1084/jem.20200164. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
39. Zoller EE, Lykens JE, Terrell CE, et al. Hemophagocytosis causes a consumptive anemia of inflammation. J Exp Med. 2011;208:1203–1214. doi: 10.1084/jem.20102538. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
40 Wang, W., Knovich, M. A., Coffman, L. G., Torti, F. M., & Torti, S. V. (2010). Serum ferritin: Past, present and future. Biochimica et Biophysica Acta (BBA) - General Subjects, 1800(8), 760-769. https://doi.org/10.1016/j.bbagen.2010.03.011
41. Kell DB, Pretorius E. Serum ferritin is an important inflammatory disease marker, as it is mainly a leakage product from damaged cells. Metallomics. 2014 Apr;6(4):748-73. doi: 10.1039/c3mt00347g. PMID: 24549403.