

Meta Review on the Effect of Iron Deficiency on Blood Donor

MinChuan Huang^{1a}, IPing Chen^{2b*} and ShuYing Chung^{3c}

¹ School of Computer Science, Guangdong University of Petrochemical Technology, Maoming City, Guangdong, China

² Taichung Blood Canter, Taiwan Blood Services Foundation, Xitun District, Taichung City, Taiwan

³ Dept. of Nursing, Central Taiwan University of Science and Technology, Beitun District, Taichung City, Taiwan

Abstract: More than 60% of the world's countries do not have enough blood. According to the analysis report of blood donors recorded in the 2021 annual report of the Taiwan Blood Service Foundation. Taiwan's blood donors also have hemoglobin disqualification issues, with 5.5% of them failing physical examinations before blood donation. The research method is a systematic review and comprehensive analysis of the literature. Meta-search has shown that long-term donors are faced with iron deficiency. Moderate iron intake by long-term blood donors can improve the impact on hemoglobin and ferritin. Significantly improve the delayed blood donation phenomenon of long-term blood donors.

1 INTRODUCTION

Donating blood is saving people's lives. The earth is the vital space for a community. Many countries urgently need a large amount of blood to meet their medical needs every year, but blood donors can only provide about 120 million units of blood. [1, 2, 3]

More than 60% of the 195 countries have insufficient blood supply to meet the demand for medical blood transfusion. The United States tracked more than 710,000 whole-blood donors in six blood centers, showing insufficient hemoglobin (Hb). Attempts to donate blood again due to insufficient hemoglobin (Hb) will be rejected. About 10% of blood donors delayed blood donation due to low hemoglobin.[4, 5, 6]

According to the Taiwan Blood Services Foundation's 2021 annual report, the rate of non-qualified blood donors was 10.55%. Among the people who failed to pass the physical examination before blood donation, 112204 had lower hemoglobin, accounting for 5.5% (annual report of Taiwan Blood Services Foundation (TBSF), a medical consortium legal person, 2021).[7, 8, 9]

According to the World Health Organization report, more than 200 million people are estimated to suffer from iron deficiency anemia (IDA) worldwide. Let's use the example of Taiwan. Blood donors in Taiwan will lose approximately 125 mg of iron every time they donate 250 ml of total blood.[10, 11, 12, 13]

The iron lost during blood donation is usually supplemented through daily diet. Regular long-term blood donors who lack nutritional knowledge and dietary behavior deviation are likely to cause insufficient iron intake. Long-term blood donation leads to a lack of iron

content in the body, or poor use of iron, unable to synthesize hemoglobin, and insufficient iron content in hemoglobin, resulting in anemia.[10, 14, 15]

2 IRON METABOLISM

There are many kinds of iron-filled substances, including four common forms of oral iron: ferrous sulphate, ferrous fumarate, ferrous polymaltose hydroxyde complex and ferrous gluconate. The most common iron injections are iron saccharose, iron dextran and sodium ferric gluconate. [16]

The National Department of Health of the Taiwan Ministry of Health and Welfare established the baseline iron intake in 2018. The reference daily iron intake is 15 mg for adolescents aged 13 to 18 and women aged 10 to 50 of child-bearing age. The reference daily iron intake is 10 mg for post-menopausal men and women.

The movement of iron in the human organism is an enclosed cycle. Iron in food comes in the form of iron. The main absorption locations are the duodenum and the upper jejunum. When iron is excessive, some will be transported to liver cells to form ferritine and store it.

The iron in the mucosal cells enters the lamina propria of the mucosa and immediately enters the blood after binding with the transferrin in the extravascular fluid. It mainly traverses the bone marrow to produce red blood cells. When iron is excessive, some will be transported to hepatic cells to form ferritin and store it.[17,18] Figure 1. Dynamic cycle diagram of iron.

^a h0912259520@163.com

^{b*} iping.tc@gmail.com

^c sychung@ctust.edu.tw

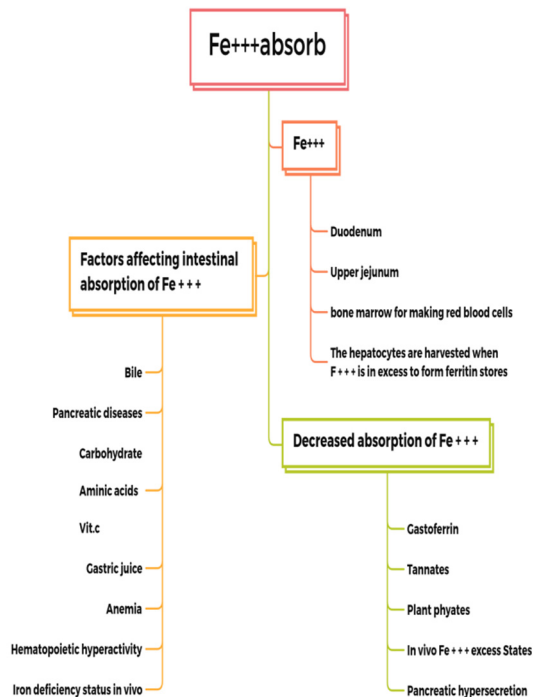


Figure 1: Dynamic cycle diagram of iron.

3 HEMOCHROME OF BLOOD DONATION

The internationally recognised normal value of hemoglobin is 13.0~18.0 g/dl for men and 10.9~15.6 g/dl for women. Taiwan's standard for healthy blood donors, the standard for blood hemoglobin concentration that can be donated, must be more than 13 g/dl for men and more than 12 g/dl for women.[19, 20]

The United States has the right to give full blood every 56 days. Female hemoglobin is greater than 12.5 g/dl and male hemoglobin is greater than 13.0 g/dl. There is no requirement for maintaining iron storage. Storing iron takes 180 days or longer to recover.[21]

Hemoglobin in women in Denmark is less than 12.5 g/dl, and hemoglobin in men is less than 13.0 g/dl, which is limited to delayed blood donation.[22, 23]

It is estimated that about 40% of people who have delayed their blood donation are because of hemoglobin that does not meet the blood donation criteria.

During the interval of blood donation, because the iron loss in the body has not yet recovered, the blood donation will be carried out again after the iron deficiency disease has occurred, which will increase the risk of anemia in the blood donor.

The study showed that every blood donation will lose 200 and 250 mg of iron, and high-frequency blood donors are inclined to consume iron reserves and iron deficiency anemia.[24] Table 1. Blood units volume & hemochromatin standards by country.

Table 1: Blood units volume & hemochromatin standards by country.

Country	Units blood donor (whole blood)	Hemochromatin criteria
China	200 ml were used as main source, Up to no more than 400 ml	Hb assay: ≥ 120 g / l in men; Female ≥ 115 g / l
Taiwan	250 ml and 500 ml	Females ≥ 12.0 g / dL Men ≥ 13.0 g / dl
France	400-480ml	Female ≥ 12.5 g/dL Men ≥ 13.5 g/dl
UK	470ml	Female ≥ 12.5 g/dL Men ≥ 13.5 g/dl
Australia	500ml	Female ≥ 12.5 g/dL Men ≥ 13.0 g/dl
U.S.	500ml	Female ≥ 12.5 g/dL Men ≥ 13.0 g/dl
Canada	450ml	Female ≥ 12.5 g/dL Men ≥ 13.0 g/dl
Switzerland	450ml	Female ≥ 12.5 g/dL Men ≥ 13.0 g/dl
Poland	500ml	Female ≥ 12.5 g/dL Men ≥ 13.5 g/dl,
GER	500ml	Female ≥ 12.5 g/dL Men ≥ 13.5 g/dl,
Netherlands	500ml	Female ≥ 12.5 g/dL Men ≥ 13.5 g/dl,

4 SYSTEMATIC LITERATURE REVIEW

4.1 SYSTEMATIC LITERATURE REVIEW RESEARCH FLOW CHART

The effect of iron supplementation by blood donors is the title, and the literature search ends in December 2022. The three major document search methods are computer database query, manual query, and expert contact in the library of the Central Taiwan University of Science and Technology. The research direction is the Cochrane Library, CINAHL, PubMed, Web of Science, EBSCOhost Web, Huayi Online Library, and National Digital Library of Theses and Dissertations Taiwan. The research process includes the literature search, the selection of literature, the inclusion and exclusion of documentation, the evaluation of documentation, assessing the quality of the literature search by two reviewers and analyzing the quality of the data.[25, 26, 27, 28] Study flow details are shown in Figure 2 Systematic literature review research flow chart.

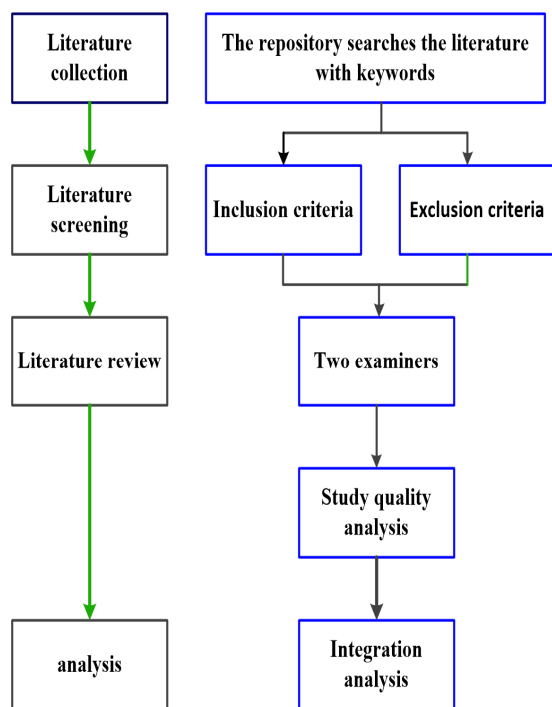


Figure 2: Systematic literature review research flow chart.

4.2 PICOS MODE

Patient Intervention Comparison Outcome Study develops questions for examination. Systematically formulate the problems to be analysed, and establish the Chinese and English keywords, which are Patient/Option: Blood donor. Comparison: No iron and no placebo were administered. Comparison: No iron and no placebo were administered. Result: Blood donors' hemoglobin is enhanced and their ferritin is effective. Study type: experimental research assigned to chance.[29, 30] Table 2. PICOS mode.

Table 1: PICOS mode.

Project	keywords
P(Patient)	Blood donor /Blood donation
I(Intervention)	Iron, Iron agent
C(Comparison)	No iron, placebo Comparison group
O1(Outcome)	Blood donor hemoglobin improvement
O2(Outcome)	Blood donor ferritin improvement
S(Study type)	RCT(control group)

4.3 EXPERT CONTACT AND MODIFIED JADAD SCALE TO EVALUATION OF RESEARCH QUALITY

By participating in professional seminars in medicine and nursing and by contacting experts, academics and authors of relevant research papers, we seek to provide suggestions for the direction of literature research. Including monographs, research papers, and minutes of meetings. Published by health and nursing agencies to

obtain pertinent information. After reading the title and summary, the screening was done. According to the purpose of the study, after reading the content of the literature, the literature was selected according to the inclusion and exclusion criteria, and then integrated into the research literature.

A systematic literature review, the quality of the search design of the selected papers was evaluated by the modified jadad scale, and the quality of the literature was evaluated by the scoring method. The two experts thoroughly extracted the documentary data and reviewed and scored each research paper, respectively.

The documents were selected based on the quality score obtained, in order to avoid the gap caused by personal subjective awareness in the research quality scoring process. If there are differences between reviewers in the document review, the third reviewer will reach consensus after discussion to assess consistency among reviewers. [31, 32]

The section text must be set to 10-point, justified and line space single.

Section, subsection and sub subsection first paragraph should not have the first line indent, other paragraphs should have a first line indent of 0,5-centimeter.

4.4 COCHRANE 2.0 DEVIATION RISK ASSESSMENT TOOL (ROB 2)

A systematic literature review was conducted to assess the quality of each research design using the amended jadad scale. The Cochrane 2.0 deviation risk assessment tool (RoB 2) was used as a reading tool to assess the quality of the deviation risk from the literature. The quality of the research and the risk of discrepancy were assessed by two independent reviewers to assess the quality and risk of the research process for each article.

The quality of each research model was measured using the modified jadad scale. The quality evaluation results of expert research are good to excellent quality, and the score range of each item in the collected documents is between 5 and 8. Among them, 8 items of extremely high quality reached 8 points.

There is one article in which the reading quality is 7.5 points. There are 2 papers with 7 points for the quality of the appraisal. There are 4 papers with 6 reading quality points.

There is an article with 5 points for the quality of the appraisal. Among them, literature # 5, respectively "whether to describe blindness", "whether to describe blindness appropriately", and # 7, "describe the number and reason of withdrawal", invited a third expert to complete the evaluation and arbitration because the readers of the two studies did not agree.

The Kappa statistical value of the quality of the research design of the collected paper samples is 0.902 P value=0.000, indicating that the review experts have significant consistency in the quality of the research included in the analysis and review literature.

5 CONCLUSIONS

The results of a meta-analysis study showed that adequate iron intake by blood donors was significantly helpful for blood donor supplementation, with a ferritin SMD of 0.735 (95% CI: 0.433 to 1.037, $p=0.000$). Studies which differentiate between women and men have yielded significant results. The SMD of iron intake on ferritin in blood donors is 0.445 (95% CI: 0.305 to 0.585, $p=0.000$).

Studies have shown that haemoglobin and ferritin values in the experimental group are superior to those in the control group. The general conclusion is that long-term blood donors should use iron appropriately, which may reduce the phenomenon of delayed blood donation caused by insufficient haemoglobin. Taking appropriate iron supplements for long-term blood donors may decrease the risk of iron deficiency.

ACKNOWLEDGEMENTS

We thank the nursing staff and the Taichung Blood Center and Taiwan Blood Services Foundation for their encouragement and support.

This project was realized with the support of the Guangdong University of Petrochemical Technology. Project Number: 2019rc076 (702-519186, 702-71013303119, 702-72100003102, 702-72200010122).

REFERENCES

- [1] Lowe, N.K. (2020) 2020 is the World Health Organization's Year of the Nurse and the Midwife. *Journal of obstetric, gynecologic, and neonatal nursing: JOGNN.* 49, 1, 1–2. DOI:<https://doi.org/10.1016/j.jogn.2019.11.008>.
- [2] Nugroho, P. et al. (2022) Comparison between the world health organization (WHO) and international society of hypertension (ISH) guidelines for hypertension. *Annals of Medicine.* 54, 1, 837–845. DOI:<https://doi.org/10.1080/07853890.2022.2044510>
- [3] Saracci, R. (1997) The World Health Organisation needs to reconsider its definition of health. *BMJ (Clinical research ed.)*.314, 7091, 1409–1410. DOI:<https://doi.org/10.1136/bmj.314.7091.1409>.
- [4] Drvenica, I.T. et al. (2022). Extracellular Hemoglobin: Modulation of Cellular Functions and Pathophysiological Effects. *Biomolecules.* 12, 11, 1708. DOI:<https://doi.org/10.3390/biom12111708>.
- [5] He, S. et al. (2021) Hemoglobin concentration is associated with the incidence of metabolic syndrome. *BMC endocrine disorders.* 21, 1, 53. DOI:<https://doi.org/10.1186/s12902-021-00719-4>.
- [6] Huehns, E.R. and Shooter, E.M. (1965) HUMAN HAEMOGLOBINS. *Journal of Medical Genetics.* 2, 1, 48–90. DOI:<https://doi.org/10.1136/jmg.2.1.48>.
- [7] Chen, Y.-Y. et al. (2019) Secular trends in the distribution of allogeneic blood components in Taiwan. *Journal of the Formosan Medical Association = Taiwan Yi Zhi.* 118, 9, 1369–1374. DOI:<https://doi.org/10.1016/j.jfma.2019.03.002>.
- [8] Shih, H. and Rajendran, S. (2019) Comparison of Time Series Methods and Machine Learning Algorithms for Forecasting Taiwan Blood Services Foundation's Blood Supply. *Journal of Healthcare Engineering.* 2019, 6123745. DOI:<https://doi.org/10.1155/2019/6123745>.
- [9] Wang, H.-H. et al. (May 2019) The alteration of ferritin and transferrin saturation under body mass index and blood pressure in first-time and regular male blood donors in Taiwan. *Medicine.* 98, 22, e15854. DOI:<https://doi.org/10.1097/MD.00000000000015854>.
- [10] Cappellini, M.D. et al. (2020) Iron deficiency anaemia revisited. *Journal of Internal Medicine.* 287, 2, 153–170. DOI:<https://doi.org/10.1111/joim.13004>.
- [11] DeLoughery, T.G. (2017) Iron Deficiency Anemia. *The Medical Clinics of North America.* 101, 2, 319–332. DOI:<https://doi.org/10.1016/j.mcna.2016.09.004>.
- [12] Lin, M. (1994) The national blood program of Taiwan, ROC. *Vox Sanguinis.* 66, 4, 299. DOI:<https://doi.org/10.1111/j.1423-0410.1994.tb00336.x>.
- [13] Tsai, S.J. and Lee, T.D. (1993) Taiwan Blood Donation Program: a model for development. *Vox Sanguinis.* 64, 3, 154–160. DOI:<https://doi.org/10.1111/j.1423-0410.1993.tb05154.x>.
- [14] Comité Nacional de Hematología et al. (2017) [Iron Deficiency and Iron Deficiency Anemia. Guideline for Prevention, Diagnosis and Treatment.]. *Archivos Argentinos De Pediatría.* 115, 4, s68–s82. DOI:<https://doi.org/10.5546/aap.2017.s68>.
- [15] Gómez-Ramírez, S. et al. (2019) Management of Perioperative Iron Deficiency Anemia. *Acta Haematologica.* 142, 1, 21–29. DOI:<https://doi.org/10.1159/000496965>.
- [16] Zhao, X. et al. (2022) Comparative Effects between Oral Lactoferrin and Ferrous Sulfate Supplementation on Iron-Deficiency Anemia: A Comprehensive Review and Meta-Analysis of Clinical Trials. *Nutrients.* 14, 3, 543. DOI:<https://doi.org/10.3390/nu14030543>.
- [17] Billesbølle, C.B. et al. (2020) Structure of hepcidin-bound ferroportin reveals iron homeostatic mechanisms. *Nature.* 586, 7831, 807–811. DOI:<https://doi.org/10.1038/s41586-020-2668-z>.
- [18] Ward, D.M. and Cloonan, S.M. (2019) Mitochondrial Iron in Human Health and Disease. *Annual Review of Physiology.* 81, 453–482.

- DOI:<https://doi.org/10.1146/annurev-physiol-020518-114742>.
- [19] Lin, P.-C. et al. (2019) Clinical Features and Genotypes of Patients with Hemoglobin H Disease in Taiwan. *Laboratory Medicine*. 50, 2, 168–173. DOI:<https://doi.org/10.1093/labmed/lmy043>.
- [20] Timoteo, V.J. et al. (2022) Positive or U-Shaped Association of Elevated Hemoglobin Concentration Levels with Metabolic Syndrome and Metabolic Components: Findings from Taiwan Biobank and UK Biobank. *Nutrients*. 14, 19, 4007. DOI:<https://doi.org/10.3390/nu14194007>.
- [21] Ahmed, M.H. et al. (2020) Hemoglobin: Structure, Function and Allostery. *Sub-Cellular Biochemistry*. 94, 345–382. DOI:https://doi.org/10.1007/978-3-030-41769-7_14.
- [22] Hulterantz, M. et al. (2020) Hemoglobin concentration and risk of arterial and venous thrombosis in 1.5 million Swedish and Danish blood donors. *Thrombosis Research*. 186, 86–92. DOI:<https://doi.org/10.1016/j.thromres.2019.12.011>.
- [23] Kotzé, S.R. et al. (2015). Predictors of hemoglobin in Danish blood donors: results from the Danish Blood Donor Study. *Transfusion*. 55, 6, 1303–1311. DOI:<https://doi.org/10.1111/trf.13011>.
- [24] Wajcman, H. and Kiger, L. (Dec. 2002). [Hemoglobin, from microorganisms to man: a single structural motif, multiple functions]. *Comptes Rendus Biologies*. 325, 12, 1159–1174. DOI:[https://doi.org/10.1016/s1631-0691\(02\)01537-8](https://doi.org/10.1016/s1631-0691(02)01537-8).
- [25] Farquhar, C. and Marjoribanks, J. (2018) Assisted reproductive technology: an overview of Cochrane Reviews. *The Cochrane Database of Systematic Reviews*. 8, 8, CD010537. DOI:<https://doi.org/10.1002/14651858.CD010537.pub5>.
- [26] Satterlee, W.G. et al. (2008) Effective medical education: insights from the Cochrane Library. *Obstetrical & Gynecological Survey*. 63, 5, 329–333. DOI:<https://doi.org/10.1097/OGX.0b013e31816ff661>.
- [27] Timmer, A. and Motschall, E. (2007) [The Cochrane Library--a short introduction for gastroenterologists]. *Zeitschrift Fur Gastroenterologie*. 45, 3, 259–264. DOI:<https://doi.org/10.1055/s-2007-962967>.
- [28] Tovey, D. (2010) The Cochrane Library is changing. *The Cochrane Database of Systematic Reviews*. 2011, ED000001. DOI:<https://doi.org/10.1002/14651858.ED000001>.
- [29] Amir-Behghadami, M. and Janati, A. (2020) Population, Intervention, Comparison, Outcomes and Study (PICOS) design as a framework to formulate eligibility criteria in systematic reviews. *Emergency medicine journal: EMJ*. 37, 6, 387. DOI:<https://doi.org/10.1136/emered-2020-209567>.
- [30] Methley, A.M. et al. (Nov. 2014) PICO, PICOS and SPIDER: a comparison study of specificity and sensitivity in three search tools for qualitative systematic reviews. *BMC health services research*. 14, 579. DOI:<https://doi.org/10.1186/s12913-014-0579-0>.
- [31] Wu, P.-L. et al. (2017) Effectiveness of physical activity on patients with depression and Parkinson's disease: A systematic review. *PloS One*. 12, 7, e0181515. DOI:<https://doi.org/10.1371/journal.pone.0181515>.
- [32] Zhang, S. et al. (2021) Effectiveness of Bundle Interventions on ICU Delirium: A Meta-Analysis. *Critical Care Medicine*. 49, 2, 335–346. DOI:<https://doi.org/10.1097/CCM.00000000000004773>.