

study the relationship between CRP and Ferritin in people infection with COVID-19 in AL-Najaf Governorate, Iraq.

Mr. Kais Khudair .Master bacteriology

kaisnoor2013@gmail.com.

assist. Prof . Maysoun khudair AL-Hadraawy

AL-Furat AL Awsat Technical University kin.msn@atu.edu.iq.

Abstract:-

Background:- Coronavirus (COVID-19) is a viral disease transmitted from person to others by coughing and sneezing droplets. COVID-19 is a new virus spread over the world symptoms of COVID-19 that can range from mild to severe disease and can develop into multi-organ failures, caused death .

Method:- The study included 68 people coming to the AL-Najaf Hospitals, who are suffering from infection by COVID-19 for a period of 2 months, from April to May month 2020. Draw 5 ml of blood for the measurement of CRP and Ferritin in patients' blood.

Result:- The current study showed that infection with Covid-19 is affected by the age factor of the patient, the age group (40-46) years was the most affected group, where the rate of infection being (38. 24).%(also, the study showed the sex factor was an effect on spread infection where the men infection was more than from women. The study also showed that the injury caused a significant increase ($p < 0.001$) in the Ferritin level in both sexes compared to the healthy group (515, 222.382) ng/ml respectively in the Men and (470, 71) ng/ml respectively in the women. also, a significant increase in CRP level compared with the healthy group (44.82,3.41) IU/ ml respectively.

Statically analysis:- The data are analyzed using by SPSS statistical program version 18 software, the categorical changeable was given as percentage and frequencies

Conclusion:- We conclude from the current study that the age and gender factor play an important role in the prevalence of Covid-19 infection and that Covid-19 infection causes an increase in both the effective protein level C and the level of the ferritin of blood , so it can be relied upon in the early diagnosis of COVID-19 infection.

Key words: CRP, COVID-19, Ferritin

introduction:

Coronaviruses are non-segmented, enveloped, positive-sense RNA viruses under a microscope that appear as a crown around a cell. Coronaviruses are found in birds, dogs, cats, whales, pigs, and humans. but more distributed in bats. (COVID-19) broke out in Wuhan, Hubei, China, and, as of early March 2020(1). it can cause serious lung inflammation and damage the digestive tract and nervous system(.2)

Virus SARS- COV caused an outbreak of acute respiratory syndrome in 2003. (1) and in 2019, the new coronavirus was revealed to be a killer and was named SARAS COV-2, which caused death to many Chinese people, and then the World Health Organization announced it was a pandemic.(3,4)

On July 2, 2020, 11 million people were infected in the world. 520,000 people died in March 2020, forcing governments to take extraordinary measures. where shops, universities, schools, and public industries were closed, travel and population

gatherings were banned and emphasized on social distancing. this is to reduce the infection rate and ensure care for all individuals infected with the virus.(5,6)

COVID-19 is a new infectious disease, it does not have treatment currently. so necessary to research biomarkers to determine the severity of the disease. COVID -19 has strong infectivity and a rate of a high incidence example CRP. CRP is one of the proteins that are made in the liver and sent to the bloodstream in response to the occurrence of inflammation and its level in the normal state is low and its height is a sign of inflammation, disease or disorder because it is considered one of the interactive indicators in the body. (7)

The disease transmitted via close contact with infected person and from respiratory droplets when an infected person talks, sneezes, or coughs .also the disease transmitted through direct contact with the contaminated surface a virus then touching eyes, nose, or mouth .

Treatment and prevention options are limited, including the use of antibody therapy, that is, the use of convalescence plasma taken from infected people after recovery from the disease, where encouraging clinical results emerged after taking this plasma and improving the chance of survival(8,9). This is because neutralizing antibodies are of particular importance as they prevent the adhesion of the virus to the surface of the cell and inhibit the fusion of the host's membrane, Consequently, rapid viral removal, which indicates that it is an anti-viral agent. As for non-neutralizing antibodies, it has a role in removing the virus according to the need for the phagocytic process mediated by the antibody-dependent cell and the antibody-dependent cellular cytotoxicity, as well as the activation of the complement.(10,11).

The current study aims to know the relationship between CRP and coronavirus infection and the effect of the infection on some blood parameters in the province of Najaf .

Methods and materials

The place of study:- Najaf Hospitals.

The studied sample:- people infected with coronavirus(covid-19) in AL Najaf city.

Study design:- a descriptive study

Period of study:- 2 months starting from April to May month 2020.

Sample size :-68 infected person coming to the Najaf Hospitals and 30 control samples.

Study steps:-clinical examination and laboratory diagnosis.

Inclusion criteria:- people infected with COVID-19.

Exclusion criteria:- people infected with other respiratory system infection.

Sample collection

a vein blood specimen was collected .in the test tube for a measure of CRP and Ferritin levels. serum was isolated after centrifugation at 3500rpm for 10 min.

CRP test:- measured CRP in patients' blood by dependent on agglutination technique and used CRP reagent[ESTEVE DE BAS-(Girona)SPAIN] with titration where titer more than 6 IU/ml considered positive.

Ferritin test:- measured the blood ferritin level was by using the VIDAS technology and diagnostic materials manufactured by company Marcy-rEloile – France.

Statically analysis:- The data are analyzed using by SPSS statistical program version 18 software, the categorical changeable was given as percentage and frequencies.

Result:-

The current study showed the relationship between the age factor and the prevalence of infection with the COVID virus-19, as the virus can infect all age

groups, but the age group (40-49) years were the most affected age (26/68), which is 38.24%.Fig.(1)

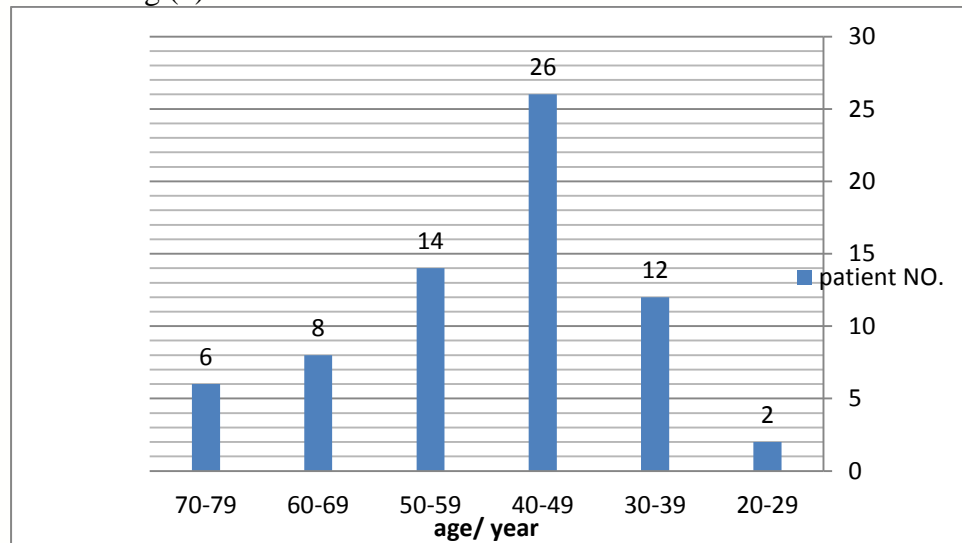


Figure (1) show the relationship between age and infection by COVID-19

The study also showed that the prevalence of coronavirus infection is influenced by gender, as males are more susceptible to infection than females, where the percentage of males was 61.76% (42/68), while the female percentage is 38.24% (26/68). Figure (2)

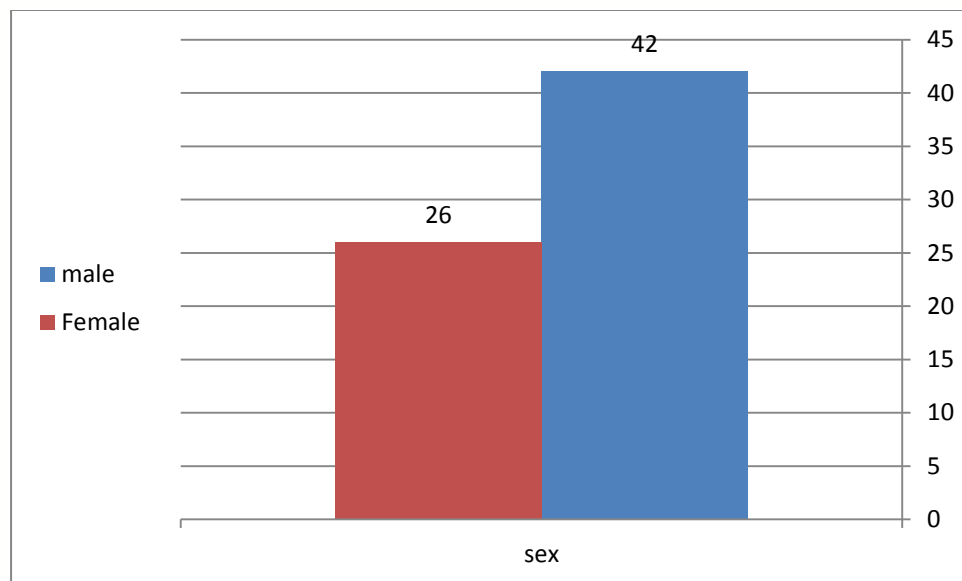


Figure (2) show the relationship between sex and infection by COVID-19.

Also, the study saw that infection with the virus Covid-19 has a significant effect on the level of the serum Ferritin(p-value <0.001) and in both sexes(515.44ng/ml in the Men, 470 ng /ml In the Female compared to the Control

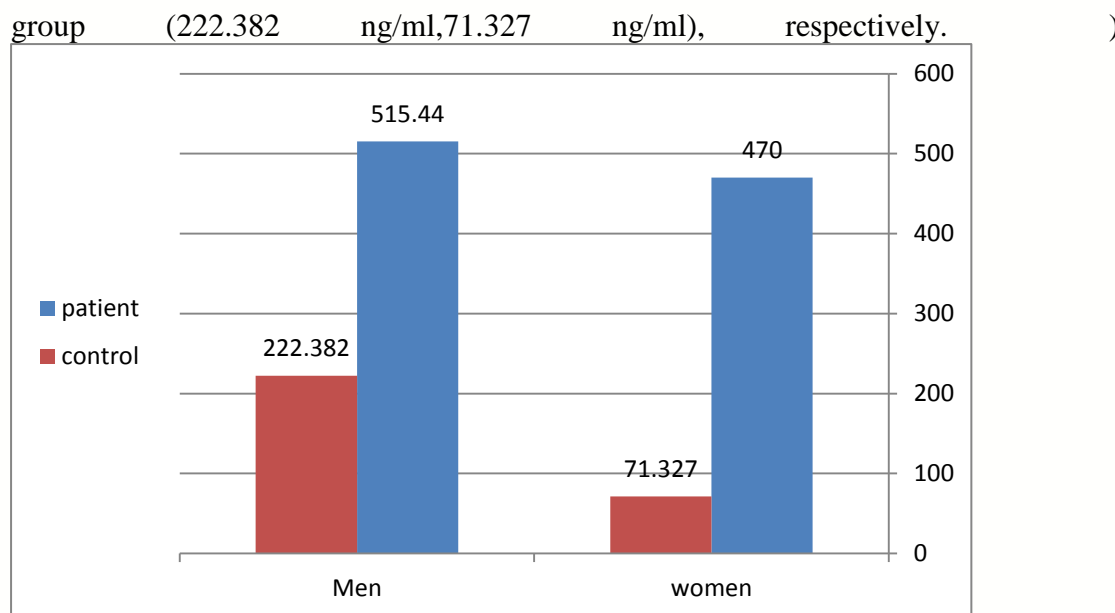


Figure (3) show the relationship between Ferritin Level and infection by COVID-19.

The current results demonstrated that coronavirus infection caused a significant increase in the level of C- Reactive Protein(p – value< 0.001 as the protein level reached (44.12 IU/ML) in infected people compared to the control group (3.41 IU / ML) Figure (4).

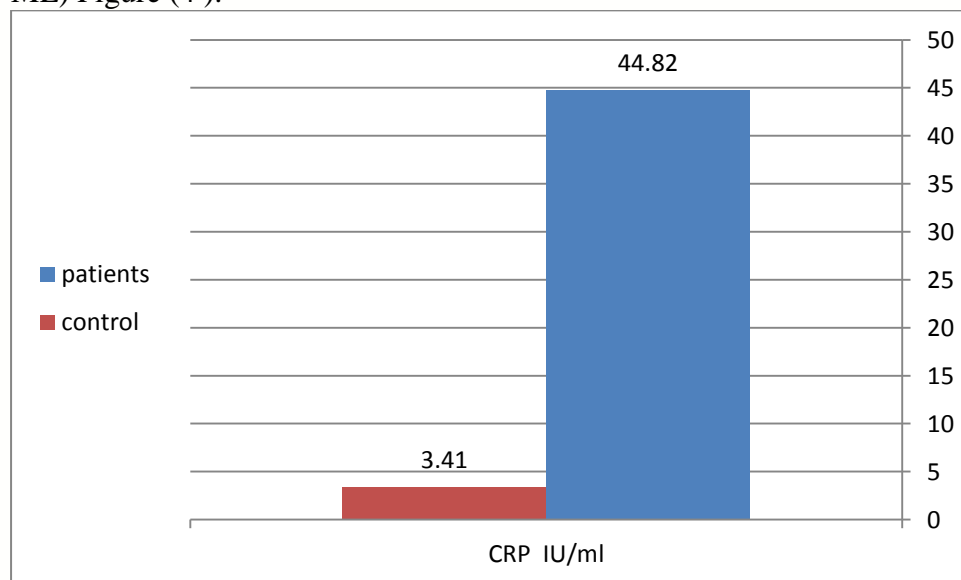


Figure (4) show the relationship between CRP Level and infection by COVID-19.

Discussion

COVID-19 pandemic is a significant general health danger that requires quick activity. Notwithstanding the extreme endeavors to discover novel medications for SARS-CoV2, this procedure is tedious with constrained advancement to date. Hence, medicate repurposing has been recognized as the quickest method of figuring it out restorative specialists for COVID-19 to meet the desperation of the situation.(12)

found many factors that affect spread infection by a coronavirus, the most important, sex and the age of the patient. the relation between sex and COVID-19 infection, where Male sex is related to the danger of increasingly extreme COVID-19 results(13), the response antibody in plasma of convalescent from men as compared

with women is amazing given women usually more immune response than men. (14) . result of the current study confirms men infection more than women this may be explained by the nature of men's work and their exposure to gatherings and mixing more than women, in addition to secondary factors such as smoking and drinking alcohol that affect the strength of the immune system in addition to the hormonal difference.

infection by coronavirus affect on a biomarker of body, as the level of CRP and Ferritin.in this study, the CRP and Ferritin levels in the serum are increased in patients with COVID-19 .this excess might cause secondary infection by bacteria and exacerbate of COVID -19 infection . in the current study evaluated levels of ferritin in the patient's serum COVID -19, which are significantly high. (15) found many studies shown that people infected by the bacterial disease had higher ferritin levels compared with infection of the virus. (16,17) the increase of ferritin levels in serum predicts a weak outcome of the hospital with infection by influenza. (18)

CRP from important of inflammatory biomarkers, CRP levels increment significantly at the beginning stage of the infection, and a positive relationship between rising CRP levels and infection severity has been depicted(19,20,21,22). [23] indicated that CRP has great analytic exactness in early foreseeing extreme COVID-19. Generally, writing proof proposes that in the beginning phase of COVID-19, CRP levels could reflect infection severity.

several studies supported our results about the level of CRP e.g. (wel Chen et. al)who demonstrated an increased level of CRP in COVID-19 infection, reaching 23.40 mg/l. so clinically depend on an increased level of CRP as an indicator of nosocomial infection COVID-19 patients who were slow to recover. (24,25)

Iron is considered one of the minerals necessary for the health of the body and plays a fundamental role in the formation of hemoglobin in the blood responsible for transporting oxygen to the cells, and it is known that its deficiency causes anemia, but its high is due to many reasons, including frequent blood transfusions or leukemia, or the reason is due to the factor Genetic. The recent study demonstrated that Covid-19 if humans affected both sexes, causes a significant increase in the level of stored iron, which explains the patient's feeling of permanent fatigue, fatigue, headache, difficulty breathing, joint pain, and general weakness(26,27).

Conclusion:-

We conclude from the current study that the age and gender factor play an important role in the prevalence of Covid-19 infection and that Covid-19 infection causes an increase in both the effective protein level C and the level of the ferritin of blood , so it can be relied upon in the early diagnosis of COVID-19 infection.

References

1. Chan JF, Yuan S, Kok KH, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. *Lancet* 2020;395:514-23.
2. Xu X, Chen P, Wang J, et al. Evolution of the novel coronavirus from the ongoing Wuhan outbreak and modeling of its spike protein for risk of human transmission. *Sci China Life Sci* 2020;63:457-60

- 3-Chen CC, Lee IK, Liu JW, Huang SY, Wang L. Utility of C-reactive protein levels for early prediction of dengue severity in adults. *Biomed Res Int.* 2015;2015:936062.
- 4-Eppy E, Suhendro S, Nainggolan L, Rumende CM. The differences between interleukin-6 and c-reactive protein levels among adult patients of dengue infection with and without plasma leakage. *Acta Med Indones.* 2016;48(1):3–9.
- 5-“Coronavirus Disease (COVID-19) Pandemic,” Mar. 2020.
[Online]. Available: <http://www.euro.who.int/en/health-topics/healthemergencies/coronavirus-covid-19/novel-coronavirus-2019-ncov>
- 6- H. Heesterbeek, R. M. Anderson, V. Andreasen, S. Bansal, D. De Angelis, C. Dye, K. T. D. Eames, W. J. Edmunds, S. D. W. Frost, S. Funk, T. Hollingsworth, T. House, V. Isham, P. Klepac, J. Lessler, J. O. Lloyd-Smith, C. J. E. Metcalf, D. Mollison, L. Pellis, J. R. C. Pulliam, M. G. Roberts, and C. Viboud, “Modeling infectious disease dynamics in the complex landscape of global health,” *Science*, vol. 347, no. 6227, Mar.2015
- 7- Huang *et.al.*2020. A retrospective analysis of the epidemiology, clinical manifestations, and imaging characteristics of familial cluster-onset COVID-19. *Ann Transl Med* 2020;8(12):747
- 8-A. Casadevall, L. A. Pirofski, The convalescent sera option for containing COVID-19. *J Clin Invest.*(2020).
- 9-K. Duan, B. Liu, C. Li, H. Zhang, T. Yu, J. Qu, M. Zhou, L. Chen, S. Meng, Y. Hu, C. Peng, M. Yuan, J. Huang, Z. Wang, J. Yu, X. Gao, D. Wang, X. Yu, L. Li, J. Zhang, X. Wu, B. Li, Y. Xu, W. Chen, Y. Peng, Y. Hu, L. Lin, X. Liu, S. Huang, Z. Zhou, L. Zhang, Y. Wang, Z. Zhang, K. Deng, Z. Xia, Q. Gong, W. Zhang, X. Zheng, Y. Liu, H. Yang, D. Zhou, D. Yu, J. Hou, Z. Shi, S. Chen, Z. Chen, X. Zhang, X. Yang, Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *Proc Natl Acad Sci U S A* **117**,9490-9496 (2020).
- 10-M. J. Joyner, R. S. Wright, D. Fairweather, J. W. Senefeld, K. A. Bruno, S. A. Klassen, R. E. Carter, A. M. Klompas, C. C. Wiggins, J. R. Shepherd, R. F. Rea, E. R. Whelan, A. J. Clayburn , M. R. Spiegel, P. W. Johnson, E. R. Lesser, S. E. Baker, K. F. Larson, J. G. Ripoll, K. J. Andersen, D. O. Hodge, K. L. Kunze, M. R. Buras, M. N. Vogt, V. Hrasevich, J. J. Dennis, R. J. Regimbal, P. R. Bauer, J. E. Blair, C. M. vanBuskirk, J. L. Winters, J. R. Stubbs, N. S. Paneth, N. C. Verdun, P. Marks, A. Casadevall, Early safety indicators of COVID-19 convalescent plasma in 5,000 patients. *J Clin Invest.* (2020)
- 11-S. J. Zost, P. Gilchuk, J. B. Case, E. Binshtein, R. E. Chen, J. X. Reidy, A. Trivette, R. S. Nargi, R. E. Sutton, N. Suryadevara, L. E. Williamson, E. C. Chen, T. Jones, S. Day, L. Myers, A. O. Hassan, N. M. Kafai, E. S. Winkler, J. M. Fox, J. J. Steinhardt, K. Ren, Y. M. Loo, N. L. Kallewaard, D. R. Martinez, A. Schafer, L. E. Gralinski, R. S. Baric, L. B. Thackray, M. S. Diamond, R. H. Carnahan, J. E. Crowe, Potently neutralizing human antibodies that block SARS-CoV-2 receptor binding and protect animals. *bioRxiv*, (2020).
- 12- Ashimiyu B. Durojaiye, John-Ross D. Clarke, George A. Stamatiades & Can Wang (2020): Repurposing cefuroxime for treatment of COVID-19: a scoping review of *in silico* studies, *Journal of Biomolecular Structure and Dynamics*, DOI: 10.1080/07391102.2020.1777904
- 13- E. P. Scully, J. Haverfield, R. L. Ursin, C. Tannenbaum, S. L. Klein, Considering how biological sex impacts immune responses and COVID-19 outcomes. *Nat Rev Immunol*, (2020).

14. K. L. Flanagan, A. L. Fink, M. Plebanski, S. L. Klein, Sex and Gender Differences in the Outcomes of Vaccination over the Life Course. *Annu Rev Cell Dev Biol* **33**, 577-599 (2017).
- 15- Kernan KF and Carcillo JA. Hyperferritinemia and inflammation. *Int Immunol*. 2017;29:401-409.
- 16- Sanaei Dashti A, Alizadeh S, Karimi A, Khalifeh M and Shoja SA. Diagnostic value of lactate, procalcitonin, ferritin, serum-C-reactive protein, and other biomarkers in bacterial and viral meningitis: A cross-sectional study. *Medicine (Baltimore)*. 2017;96:e7637.
- 17- Kawamata R, Yokoyama K, Sato M, Goto M, Nozaki Y, Takagi T, Kumagai H and Yamagata T. Utility of serum ferritin and lactate dehydrogenase as surrogate markers for steroid therapy for *Mycoplasma pneumoniae* pneumonia. *J Infect Chemother*. 2015;21:783-9.
- 18- Lalueza A, Ayuso B, Arrieta E, Trujillo H, Folgueira D, Cueto C, Serrano A, Laureiro J, Arevalo-Canas C, Castillo C, Diaz-Pedroche C, Lumbreras C and group I. Elevation of serum ferritin levels for predicting a poor outcome in hospitalized patients with influenza infection. *Clin Microbiol Infect*. 2020.
19. Yang W, Cao Q, Qin L, Wang X, Cheng Z, Pan A, et al. Clinical characteristics and imaging manifestations of the 2019 novel coronavirus disease (COVID-19): a multi-center study in Wenzhou city, Zhejiang, China. *J Infect* 2020;80:388–93.
20. Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *J Am Med Assoc* 2020;323:1061–69. <https://doi.org/10.1001/jama.2020>.
21. Matsumoto H, Kasai T, Sato A, Ishiwata S, Yatsu S, Shitara J, et al. Association between C-reactive protein levels at hospital admission and long-term mortality in patients with acute decompensated heart failure. *Heart Ves* 2019;34:1961–8.
22. Wang L. C-reactive protein levels in the early stage of COVID-19. *Med Mal Infect* 2020; 50:332–4. <https://doi.org/10.1016/j>.
23. Tan C, Huang Y, Shi F, Tan K, MaQ, Chen Y, et al. C-reactive protein correlates with CT findings and predicts severe COVID-19 early. *J Med Virol* 2020. <https://doi.org/10.1002/jmv.25871>
24. Feng G, Zheng KI, Yan QQ, Rios RS, Targher G, Byrne CD, et al. COVID-19 and liver dysfunction: current insights and emergent therapeutic strategies. *J Clin Transl Hepatol*. 2020;8(1):1–7.
25. Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX, et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020;382(18):1708–20.
26. Abbaspour N, Hurrell R, Kelishadi R. Review on iron and its importance for human health. *Research J Med Sci*. 2014;19(2):164–74.
- 27-Fleming DJ, Tucker KL, Jacques PF, Dallal GE, Wilson PWF, Wood RJ. Dietary factors associated with the risk of high iron stores in the elderly Framingham Heart Study cohort. *Am J Clin Nutr*. 2002;76:1375–84.