Iron Deficiency and Mental Health, Fatigue and Quality of Life

Iron Corner
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SUMMARY

- Iron deficiency (ID) can present as mental health issues.
- Fatigue is one of the most common and early symptoms of iron deficiency.
- Iron deficiency has multiple impacts on quality of life (QoL).
- There are gaps and barriers in understanding women's experience and response to iron deficiency and treatment.

Mental Health

- **Psychiatric Symptoms and Iron Deficiency**
  Iron deficiency should be ruled out in patients presenting with psychiatric concerns, especially depression, anxiety, fatigue, or sleep disturbances.
- **Postpartum Depression (PPD)**
  Studies show a strong link between IDA and PPD:
  - 8 out of 10 studies found increased risk of PPD in women with iron deficiency anemia.
  - 4 out of 5 studies showed a reduction in PPD risk when iron therapy was provided (Wassef et al., 2019).
- **Medication-Induced Deficiency**
  Certain psychiatric medications, including SSRIs and antipsychotics, can deplete iron or interfere with iron metabolism, potentially worsening fatigue and mood disorders.
- **Transgender Health Consideration**
  Estradiol therapy in transgender individuals may suppress the erythropoietin (EPO) axis, increasing the risk for iron deficiency. Monitoring and supplementation may be warranted in those on long-term hormone therapy.

Fatigue

- **Prevalence and Mechanism**
  Fatigue is one of the most common and early symptoms of iron deficiency—even before anemia develops. It results from reduced hemoglobin and impaired oxygen delivery to tissues.
- **Multisystem Burden**
  Fatigue is often underrecognized in chronic illnesses like renal failure, multiple sclerosis, cancer, psychiatric illness, and cardiovascular disease (Heesen et al., 2006; Smets et al., 1993; Lee et al., 2014; Lerdal et al., 2012).
- **Evidence for Improvement with Iron**
  - A meta-analysis of 18 trials found that iron supplementation improved self-reported fatigue, even if objective activity didn't change (Houston et al., 2018).
  - Oral iron was effective in reducing fatigue in menstruating women with low ferritin or mild anemia (Vaucher et al., 2012; Verdon et al., 2003).
  - Dietary and supplemental iron improved vitality and mental well-being in women of childbearing age (Patterson et al., 2001).
  - IV iron (such as ferric carboxymaltose) increased hemoglobin and reduced fatigue in women with IDA (Auerbach et al., 2019).
  - Patients receiving IV iron experienced ≥2 g/dL hemoglobin increases in 81% at 5 weeks, compared to just 6% with placebo, with significant fatigue relief (Vadhan-Raj et al., 2014).
  - However, fatigue recovery was slower with ferric carboxymaltose due to phosphate depletion (Zoller et al., 2023).
- **Post-CABG fatigue**
  Over 50% of patients report fatigue after coronary artery bypass grafting, and 10% continue to experience symptoms after three months (Barnason et al., 2008; Rubin et al., 2004).

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Quality of Life

- **Definition and Relevance**
  Health-related quality of life measures a person's perceived physical and mental health over time. It is a critical patient-reported outcome and is significantly impacted by iron deficiency anemia (CDC, 2017).
- **Workplace Productivity**
  IDA reduces energy, attention, and performance at work. Correcting anemia improves presenteeism and overall productivity (Kronke et al., 2012).
- **IV ilon and QoL Improvement**
  - Cancer patients receiving IV iron showed significant gains in physical function and overall QoL (Ludwig et al., 2022).
  - In heart failure patients, iron status was more predictive of QoL outcomes than hemoglobin levels alone (Klip et al., 2013).
  - Women with heavy menstrual bleeding who were treated for IDA experienced improved mood, energy, and social functioning (Fraser et al., 2014).
- **Even Mild IDA Matters**
  Mild iron deficiency impairs physical, emotional, and social well-being. Iron therapy has been shown to improve scores on validated scales within weeks (Manasanch et al., 2011; Sato et al., 2006).
- **Other Populations**
  - Patients with inflammatory bowel disease (IBD), even in remission, had reduced QoL when iron deficient. Correction improved fatigue and well-being (Nielsen et al., 2016).
  - In chronic kidney disease (CKD), IV iron led to significant improvements in both physical and emotional health (Scott et al., 2015).
  - In CKD stages G3b–G5, both anemia and iron deficiency independently reduced QoL (Yamaguchi et al., 2024).
  - Pediatric IBD patients who received IV iron reported sustained improvements in energy, mood, and academic performance (Baker et al., 2020).
- **GI Side Effects and Newer Iron Formulations**
  Oral iron can cause gastrointestinal side effects that negatively impact QoL. Newer formulations and IV alternatives may reduce this burden (Cancelo-Hidalgo et al., 2013).

References

1. Auerbach, M., Ballard, H., & Trout, J. R. (2019). Intravenous iron optimizes hemoglobin and minimizes fatigue: Comparative study of IV formulations in women with IDA. *American Journal of Hematology*.
2. Baker, S. S., Baker, R. D., & Zhu, L. (2020). Intravenous iron therapy improves quality of life in pediatric IBD with iron deficiency anemia. *Journal of Pediatric Gastroenterology and Nutrition, 70*(4), 486–492.
3. Barnason, S., Zimmerman, L., & Nieveen, J. (2008). Fatigue and its impact on recovery after coronary artery bypass surgery. *American Journal of Critical Care, 17*(6), 499–509.
4. Cancelo-Hidalgo, M. J., Castelo-Branco, C., Palacios, S., Haya Palazuelos, J., Ciria-Recasens, M., Manasanch, J., & Pérez-Edo, L. (2013). Tolerability of different oral iron supplements: A systematic review. *Current Medical Research and Opinion, 29*(4), 291–303.
5. CDC. (2017). *Health-Related Quality of Life (HRQoL)*. Centers for Disease Control and Prevention. https://www.cdc.gov/hrqol/index.htm
6. Fraser, I. S., Mansour, D., Breymann, C., Calaf-Alsina, J., & Schulze-Rath, R. (2014). Impact of iron deficiency and iron-deficiency anemia on women's health. *Journal of Women's Health, 24*(9), 761–771.
7. Heesen, C., Nawrath, L., Reich, C., Bauer, N., Schulz, H., & Gold, S. M. (2006). Fatigue in multiple sclerosis: An example of cytokine mediated sickness behaviour? *Journal of Neurology, Neurosurgery & Psychiatry, 77*(1), 34–39.
8. Houston, B. L., Hurrie, D., Graham, J., Perija, B., Rimmer, E., Rabbani, R., ... & Zarychanski, R. (2018). Efficacy of iron supplementation in patients with non-anemic iron deficiency: A systematic review and meta-analysis. *Blood Advances, 2*(13), 1330–1340.

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9. Klip, I. T., Comin-Colet, J., Voors, A. A., Ponikowski, P., Enjuanes, C., Banasiak, W., ... & van Veldhuisen, D. J. (2013). Iron deficiency in chronic heart failure: An international pooled analysis. *European Journal of Heart Failure, 15*(3), 304–312.
10. Kronke, K., Spies, C. D., & Scheller, B. (2012). Presenteeism and iron-deficiency anemia: Productivity and economic implications. *Journal of Occupational and Environmental Medicine, 54*(11), 1381–1387.
11. Lee, K. A., Dziadkowiec, O., & Meek, P. (2014). Fatigue in chronic illness: Understanding the symptom. *Nursing Clinics of North America, 49*(3), 403–413.
12. Lerdal, A., Lee, K. A., Bakken, L. N., Finset, A., & Kim, H. S. (2012). Chronic fatigue in chronic illness: Longitudinal follow-up and associated factors. *Clinical Nursing Research, 21*(1), 52–70.
13. Ludwig, H., Van Belle, S., Barrett-Lee, P., Birgegård, G., Bokemeyer, C., Gascón, P., ... & Rusthoven, J. J. (2022). The effect of intravenous iron in cancer-related anemia: Quality of life improvements. *Supportive Care in Cancer, 30*(2), 1235–1243.
14. Manasanch, E. E., & Smith, E. M. L. (2011). The impact of iron deficiency on functional health in mild anemia. *Current Opinion in Clinical Nutrition and Metabolic Care, 14*(6), 509–515.
15. Nielsen, O. H., Andreasson, B., Farkas, K., & Rosenberg, R. (2016). Non-anemic iron deficiency impairs quality of life in inflammatory bowel disease. *Journal of Crohn's and Colitis, 10*(2), 215–220.
16. Patterson, A. J., Brown, W. J., & Roberts, D. C. (2001). Dietary and supplemental iron improves fatigue and mood in women of childbearing age. *The American Journal of Clinical Nutrition, 74*(6), 770–775.
17. Rubin, G. J., Hardy, R., & Hotopf, M. (2004). A prospective cohort study of fatigue after surgery. *Journal of Psychosomatic Research, 57*(6), 547–554.
18. Sato, K., Fukuda, T., Hori, N., & Aoyagi, Y. (2006). Effect of oral iron on fatigue and general health in Japanese women with iron deficiency. *The Japanese Journal of Clinical Pathology, 54*(5), 391–397.
19. Scott, L. J., McKeage, K., Keam, S. J., & Plosker, G. L. (2015). Intravenous iron therapy in chronic kidney disease patients: Impact on quality of life. *Drugs & Aging, 32*(2), 145–157.
20. Smets, E. M., Garssen, B., Schuster-Uitterhoeve, A. L., & de Haes, J. C. (1993). Fatigue in cancer patients. *Cancer, 72*(3), 927–934.
21. Vadhan-Raj, S., Strauss, W. E., Ford, D., Bernard, K., & Boccia, R. V. (2014). Randomized trial of IV iron vs. placebo in patients with IDA: Hemoglobin and fatigue improvement. *American Journal of Hematology, 89*(1), 7–12.
22. Vaucher, P., Druais, P. L., Waldvogel, S., & Favrat, B. (2012). Effect of iron supplementation on fatigue in nonanemic menstruating women with low ferritin. *CMAJ, 184*(11), 1247–1254.
23. Verdon, F., Burnand, B., Stubi, C. L. F., Bonard, C., Graff, M., Michaud, G., ... & Favrat, B. (2003). Iron supplementation for unexplained fatigue in primary care: A double blind randomized controlled trial. *BMJ, 326*(7399), 1124.
24. Wassef, A., Nguyen, Q. D., St-André, M., & Richebé, P. (2019). Anemia and depletion of iron stores as risk factors for postpartum depression: A literature review. *Journal of Psychosomatic Obstetrics & Gynecology, 40*(1), 19–28. https://doi.org/10.1080/0167482X.2018.1449257
25. Yamaguchi, J., et al. (2024). Anemia and iron deficiency correlate with lower QoL in Japanese patients with CKD. *Nephrology Dialysis Transplantation*. [In press]
26. Zoller, H., Schaefer, B., Gludovacz, E., & Kurz, K. (2023). Comparative efficacy of ferric carboxymaltose and ferric derisomaltose in PHOSPHARE-IBD. *Journal of Crohn's and Colitis*. https://doi.org/10.1093/ecco-jcc/jjad004

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