

The Institute for Integrative and Functional Pathology



Holistic and nutritional pathology analysis training for health practitioners

Guidelines on iron tests, iron deficiency and iron overload.

This article is a reminder for health practitioners who check blood test results, including GPs, doctors, Nutritionists, Naturopaths, Dietitians, Allied Health practitioners, and others. This information and advice is especially related to the Iron Studies test and its biomarkers.

Please remember this – you CANNOT determine if a patient has an iron deficiency or overload just from checking the Serum Ferritin test result!

Despite what you may have been taught in college, university, or from other sources, Ferritin is NOT the main or best test for a patient's iron status. The full Iron Studies test MUST be done (ie, serum iron, TIBC and/or Transferrin, Transferrin Saturation and Ferritin), and ALL of the Iron Studies test results must be checked and interpreted TOGETHER!

Too many times we have seen practitioners, including doctors/GPs and others, suggesting that a patient has an iron deficiency or overload issue just from Ferritin alone, but all the other iron results indicate the opposite diagnosis. If the wrong diagnosis is made, such as an iron deficiency when in fact the patient has all the signs of an iron overload but with low Ferritin, the prescribed treatment of iron supplements and/or iron infusions can make the patient's symptoms much worse.

Ferritin might be the iron storage protein within the cells. But it's not an accurate measurement of iron storage, as the Ferritin level is greatly affected by infections as a self-defence mechanism, to slow down bacterial infections by sequestering the iron being transported around the body by Transferrin, and binding it to Ferritin inside cells. This prevents the bacteria from using the iron, which they need for reproduction, and to spread the infection. This results in a lower Transferrin Saturation level, but higher Ferritin due to infections.

Ferritin is an acute phase reactant marker due to increased inflammation, which causes higher Ferritin and lower Transferrin Saturation. This can push up the Ferritin level from "low", even from lower than the lab's reference range, and up into the reference range or even higher than the reference range. Even if the patient's iron levels are low.

Ferritin is also affected by oxidative damage and tissue damage, which can push a low Ferritin result into the reference range, or even an optimal Ferritin result higher than the reference range. Again, even with low iron levels.

Another major point about Ferritin – why are we measuring or interpreting **Serum** Ferritin?! If Ferritin is the storage protein for iron INSIDE the cells, what is it doing outside in the serum?! Studies show that the Serum Ferritin is there due to cellular damage, which causes the cells to split open and

release their contents, including Ferritin. This is most likely why infections, inflammation, oxidative damage cause cellular lysis, splitting them open and releasing the Ferritin and causing high levels in these situations. As such, how relevant is Serum Ferritin to a patient's iron status? Very limited. Hence the need to look at ALL the iron related biomarkers in the Iron Studies test, but also the FBC/FBE test, and others to confirm either an iron deficiency, iron overload, or optimal iron levels. Even the RACGP suggests that 90% of high Ferritin results is not due to iron levels (RACGP, 2012).

Pathology analysis is an art and a science, of interpreting multiple test results together, and not just diagnosing based on one test result alone. Otherwise mistakes in diagnosis and prescribing can occur.

Hence why it's essential to check all the Iron Studies test results to either confirm whether the patient has a true iron overload issue, or even an iron deficiency. Also you need to check the FBC/FBE test to check for anaemia and infections, and the CRP and ESR tests to check for inflammation.

In the IIFP pathology analysis training courses for practitioners, for better analysis and interpretation of pathology results, we explain the issues of using the lab's reference ranges, and we show why "optimal" ranges are best for getting accurate findings from a patient's results.

Here's some real case studies and findings and recommendations:

Situation 1:

A new patient, 38yo female, presents with mental exhaustion, brain fog, dizziness, and hormone/cycle issues.

I checked her previous pathology results, which were almost 18 months earlier, to find possible causes of her exhaustion – FBC, iron studies, thyroid, and more.

Her GP did some basic tests but had only previously tested her Ferritin, and not the full Iron Studies test. I recommended the full test, and her results were as follows:

| CUMULATIVE IRON STUDIES | | | |
|-------------------------|----------|----------|---------------|
| Date | 20/06/24 | 01/12/25 | |
| Time | 09:52 | 09:16 | |
| Lab No | | | |
| Iron | 29 | umol/L | (10-33) |
| TIBC | 66 | umol/L | (45-70) |
| Saturation | 44 | % | (16-50) |
| Ferritin | 33 | 18 | ug/L (25-290) |

The patient had previously been diagnosed with low iron because of low Ferritin results, and she was prescribed the Maltofer supplement to be taken daily, which didn't really help her mental exhaustion.

Looking at the full Iron Studies results which were done in a fasted state, and using optimal ranges instead, we note the following:

1. Serum Iron – is higher than the optimal range, indicating a high intake of iron in the last meal before the test. This can also indicate recent iron supplementation or iron infusion, but we made sure that she had stopped taking any iron supplement for a number of days before testing – but as the iron supplement hadn't been working, she had not been taking this for a while anyway. Hence this is a possible iron overload result.
2. TIBC – Is higher than the optimal range, which typically can indicate and iron deficiency, OCP use, polycythaemia vera, or other causes.
3. Transferrin Saturation – is higher than the optimal range. This indicates an iron overload condition, recent iron supplements or infusion (ruled out), or heavy exercise before testing.
4. Serum Ferritin – is lower than the optimal range, which can suggest either low protein levels (from low intake or poor stomach function) as ferritin is a protein, or low thyroid or liver function, low zinc, or other causes.

In these results we have two biomarkers indicating an iron overload, and two suggesting an iron deficiency. In her other results, TSH was high and indicating a hypothyroid state, and zinc was quite low. These two factors can explain why the Ferritin is low.

Another likely explanation for the low Ferritin with the iron overload results is that at her age (38yo) the possible iron overload (ie, Haemochromatosis) is at an early stage and has not become pathological to cause any tissue damage from the oxidative stress from the high iron levels.

I have recommended that she get the HFE genetic test for haemochromatosis. Results are not available as yet.

Situation 2:

A recent patient, 52yo female, presents with poor memory and cognition, mentally overwhelmed, muscle aches, hair loss, and unable to work because of these symptoms.

Blood tests from the GP earlier (Dec 2024) showed anaemia (low Haemoglobin), hypothyroid (high TSH, low T4 and T3), history of leukopenia, low protein levels (as a vegetarian), and a history of low Ferritin.

Her Iron Studies/Haematinics results are as follows:

| Haematinics | 22-Nov-23 | 22-Jan-24 | 06-Mar-24 | 01-Jul-24 | 31-Dec-24 | Latest Results | |
|-------------|-----------|-----------|-----------|-----------|-----------|----------------|-----------|
| | 07:54 | 12:23 | 08:27 | 08:30 | 07:52 | 25-Aug-25 | Reference |
| | 684528053 | 684528821 | 684523460 | 527836101 | 530523591 | 533844513 | |
| Iron | 12 | 14 | 13 | 30 | 54 H | 29 | (5-30) |
| Transferrin | 1.9 | 1.9 | 1.8 L | 2.1 | 2.2 | 2.1 | (1.9-3.1) |
| TIBC | 49 | 48 | 44 L | 52 | 55 | 52 | (47-77) |
| Trans Sat | 24 | 29 | 30 | 58 H | 98 H | 56 H | (20-45) |
| Ferritin | 21 L | 24 L | 25 L | 15 L | 14 L | 23 L | (30-300) |

Comments about her results:

1. Serum Iron – The first 3 results are optimal, but then something changed after the March 2024 results where the result more than doubled, then almost doubled again... indicating an increased iron absorption and iron overload
2. Transferrin – The first 3 results are low, either due to an iron overload, or due to inflammation as a negative acute phase reaction
3. TIBC – Mostly optimal results, with the exception to the March 2024 result being low, and indicating an iron overload situation
4. Transferrin Saturation – The first 3 results are optimal, then the results doubled and doubled again, so the last 3 results are all very high, higher than the optimal upper limit, and indicating an iron overload or other causes, but absolutely NOT an iron deficiency
5. Serum Ferritin – ALL results are low, with the 3rd to 5th results getting progressively worse. Analysing all the iron results together indicate a strong iron overload issue, and NOT an iron deficiency at all, even with the low Ferritin result.

In this case, again, the very low Ferritin would have been from the low protein levels (confirmed), low zinc (confirmed), and low thyroid function (confirmed). Liver function was optimal. Similar to the first case, the iron overload (ie, Haemochromatosis) could be at an early stage and has not become pathological to cause any tissue damage as yet.

The GP recommended an iron infusion, based on the very low Ferritin result (of Dec 2024), completely ignoring the extremely high Serum Iron indicating an iron overload condition, which was confirmed with the extremely high Transferrin Saturation of 98%!

Her symptoms did not improve from the iron infusion.

Based on these results and the patient's symptoms, I recommended she get the HFE genetic test for Haemochromatosis. Her results were as follows:

| Haemochromatosis Genotyping | |
|--|---|
| Specimen | EDTA Blood |
| C282Y | Heterozygous Mutation Detected * |
| H63D | Heterozygous Mutation Detected * |
| Comments: | |
| This patient is compound heterozygous for the HFE: c.845G>A, p.Cys282Tyr and HFE: c.187C>G, p.His63Asp mutations. | |
| This genotype, when found in conjunction with evidence of iron overload (persistent hyperferritinaemia and transferrin saturation >45%) may be consistent with a diagnosis of HFE-associated haemochromatosis. However other causes of hyperferritinaemia, including inflammatory states (e.g. infection, autoimmune conditions, malignancy) and liver pathology (e.g. viral hepatitis, alcohol-related liver disease and non-alcoholic fatty liver disease) should be excluded. | |

The patient was an unknown carrier of two of the HFE genetic mutations for Haemochromatosis! This combination of Iron Studies results and HFE testing shows that HFE carriers CAN have significant effects to their Iron Studies results and therefore on a patient's symptoms.

Having an iron overload issue causing a lot of oxidative damage in her body, and then taking an iron infusion with a high dose of iron, causes even more oxidative damage especially to the brain, and hence her symptoms.

It took so many messages to the GP to understand that this mutual patient CAN have anaemia and an iron overload at the same time. This is because anaemia isn't always about iron. An iron deficiency anaemia is one of many types of anaemia.

Situation 3:

A recent patient of a fellow practitioner (ie, not my patient initially), 43yo female, presents with low energy and fatigue, and headaches.

A GP ran some blood tests, and her Iron Studies results were as follows:

| Date: | | 29/04/25 | 30/05/25 | 01/07/25 | | |
|-------------|--------|---------------|---------------|---------------|-------------|--------------|
| Lab Number: | | 34040324 | 34847141 | 35554992 | | |
| | | | | | Ref. | Range |
| Serum Iron | umol/L | 8 * | 21 | 6 * | | (10 - 30) |
| Transferrin | g/L | 1.7 * | 1.8 * | 1.8 * | | (2.0 - 3.5) |
| Transf sat | % | 19 | 46 | 13 * | | (16 - 50) |
| Ferritin | ug/L | 1110 * | 1246 * | 1112 * | | (20 - 350) |

Some thoughts on these results:

1. Serum Iron - Low results in the first and third tests indicate a low iron intake. On questioning, the patient was given a blood transfusion and beef liver supplements before the second test, due to severe anaemia. Hence why the higher Serum Iron, too-high Transferrin Saturation and higher Ferritin at that time, before the iron levels dropped again.
2. Transferrin - Low in all results indicates either an iron overload or inflammation, as Transferrin is a negative acute phase reactant marker.
3. Transferrin Saturation - Below the minimum optimal range for the first and third results, suggesting either an iron deficiency or iron being sequestered away from Transferrin to Ferritin due to infections and/or inflammation.

The patient's GP diagnosed her with having Haemochromatosis after the first high Ferritin result, but did NOT confirm this with the HFE genetic test! They based this diagnosis on her elevated Ferritin result only. As such, the GP recommended blood venesections, and the patient's Nutrition Therapist (untrained in pathology analysis) followed along with the diagnosis, and recommended the patient avoid iron-rich foods such as red meats, and even recommended some iron-chelating herbs and supplements.

The Nutrition Therapist asked the IIFP for advice on the patient's test results. Based on these results and others, our interpretation of the results was that the patient likely has an iron deficiency, but

also has an acute infection and/or inflammation and/or oxidative damage, which is causing the elevated Ferritin result.

The recommended blood venesections and chelation therapy need to stop immediately, and the patient needs to INCREASE their iron intake, improve stomach and digestive system functions to improve iron absorption, and other treatments to reduce inflammation and support immune system function to reduce the Ferritin level.

Both the GP and NT likely made the patient's symptoms worse due to incorrect and incomplete analysis of the blood test results, and putting both of them in a difficult position of having to explain to the patient how they both got the diagnosis and treatment plan completely wrong.

Conclusion:

These real case examples all show that you cannot determine an iron deficiency or overload just with looking at the patient's Serum Ferritin test result. ALL the Iron Studies results, and even other test results are needed to confirm or rule out an iron deficiency or overload presentation.

The common belief that a low Serum Ferritin result is indicating an iron deficiency, or high Ferritin indicating an iron overload, MUST be dismissed. As must also be dismissed the belief that being an HFE/Haemochromatosis carrier is a benign condition, does not cause any iron overload presentation in blood test results or symptoms. Sadly, we have seen far too many HFE carrier patients with moderate to severe iron overload results and symptoms.

What also must be understood is that a patient CAN have an iron overload and anaemia at the same time! And that Haemochromatosis is a progressive presentation of symptoms – causing high iron results when triggered, in both those with the full homozygous presentation or even the heterozygous presentation, together with low or optimal Ferritin initially. Only when the iron levels become high enough to cause oxidative damage, and cellular damage, will the Ferritin be lysed from the red blood cells to cause the high Ferritin results and other abnormal results to pancreatic, liver, and heart functions, and others too.

For more information on pathology analysis and training courses for health practitioners, please visit the IIFP (Institute for Integrative and Functional Pathology) website here – www.pathologyanalysis.com

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