15. RAISED SERUM FERRITIN

15.1 SCOPE

Serum ferritin is derived from intracellular ferritin which is responsible for the dynamic storage of iron within the cell. Ferritin exists in all cells, but highest levels are seen with macrophages of the bone marrow and liver – the predominant storage sites of body iron.

Ferritin within the serum is a subunit of intracellular ferritin. It is actively excreted from cells and has no role in iron transport. In steady state the quantity in the serum is proportional to the quantity in storage cells. This means that serum ferritin is proportional to the body iron content. However, in the setting of infection and inflammation, more ferritin is lost from cells and serum ferritin is no longer proportional to body iron content.

15.2 ASSESSMENT

A serum ferritin below 15mcg/l is indicative of absolute iron deficiency

A normal serum ferritin does not exclude iron deficiency, particularly where there is infection or inflammation

A raised serum ferritin is identified as follows:

- Above 200mcg/l in women and above 300mcg/l in men

15.3 MANAGEMENT

Most raised ferritins seen in primary care are due to infection or inflammation.

Do not refer for advice for a raised ferritin without the result of transferrin saturation.

Do not refer for isolated raised serum iron without a raised transferrin saturation.

Do not refer isolated raised T sats if ferritin is normal.

- If serum ferritin above 200mcg/l and Tsat% above 40% in Women request HFE gene mutation analysis on an EDTA sample
- If serum ferritin above 300mcg/l and Tsat% above 50% in Men request HFE gene mutation analysis on an EDTA sample
- If HFE gene analysis shows homozygosity for the C282Y mutation, refer to Hepatology for management of Genetic Haemochromatosis in line with published guidance: https://onlinelibrary.wiley.com/doi/pdf/10.1111/bjh.15164
- If the serum ferritin is elevated without elevation of the transferrin saturation this indicates that the cause is NOT iron overload.
- Suggest further investigation and management in line with published guideline: Investigation and management of a raised serum ferritin (wiley.com) https://onlinelibrary.wiley.com/doi/epdf/10.1111/bjh.15166

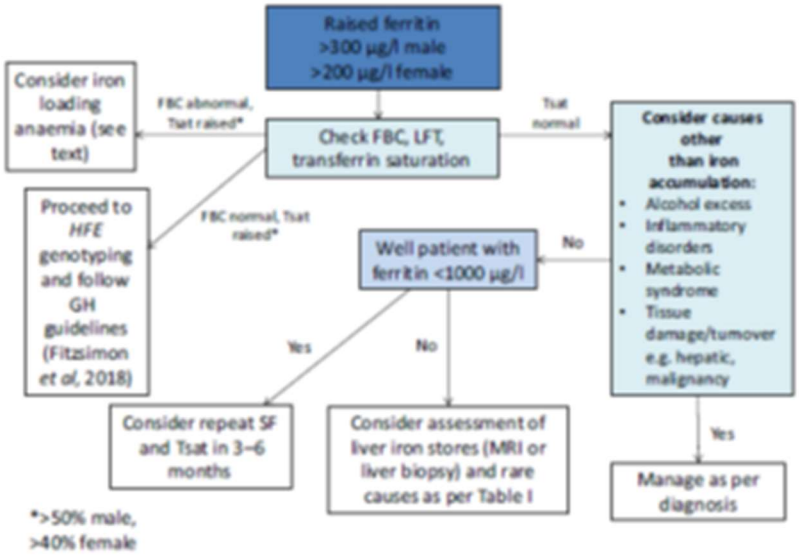

Fig 1. Suggested algorithm for investigation of isolated elevated serum ferritin levels in patients without known secondary iron overload. FBC, full blood count; GH, genetic haemochromatosis; LFT, liver function tests; MRI, magnetic resonance imaging; SF, serum ferritin; Tsat, transferrin saturation.

Table I. Causes of raised serum ferritin.

Increased ferritin synthesis due to iron accumulation	Increase in ferritin synthesis not associated with significant iron accumulation	Increased ferritin as a result of cellular damage
Hereditary (genetic) haemochromatosis	Malignancies	Liver diseases including liver necrosis, chronic viral hepatitis, alcoholic and non-alcoholic steatohepatitis*
Hereditary acaeruloplasminaemia	Malignant or reactive histiocytosis	Chronic excess alcohol consumption
Secondary iron overload from blood transfusion or excessive iron intake/administration	Hereditary hyperferritinaemia with and without cataracts	
Ineffective erythropoiesis: sideroblastic anaemia, some myelodysplastic syndromes (e.g. refractory anaemia with ring sideroblasts)	Gaucher disease	
	Acute and chronic infections	
	Chronic inflammatory disorders	
	Autoimmune disorders	
Thalassaemias		
Atransferrinaemia		
Ferroportin disease		

*May also have iron overloading.