# COVID-19 lockdown measures induced severe iron-deficiency anaemia resulting in central retinal vein occlusion and amenorrhea

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## SUMMARY

During the COVID-19 pandemic, precautionary measures taken by various countries include individual movement restrictions causing significant lifestyle changes and affecting dietary patterns. A 23-year-old woman presented with reduced left eye vision over 1 week and amenorrhea for 4 months. She was diagnosed with severe iron-deficiency anaemia causing central retinal vein occlusion and amenorrhea. During the lockdown, there was a change in her diet with greatly reduced iron intake. Iron is an essential mineral for retina metabolism and function. Iron supplementation was done with improvement in her vision. This case demonstrates the potential impact of lockdown measures on nutrition and health. Education of the general population on maintaining appropriate nutrition during periods of movement restriction is important and that nutritional evaluation and supplementation should be considered in patients with drastic changes in dietary pattern.

## BACKGROUND

Central retinal vein occlusion (CRVO) is a common retinal vascular disease.[1] The pooled 10-year global cumulative incidence of retinal vein occlusion is 1.63%.[2] Cases of iron-deficiency anaemia (IDA)-induced CRVO were previously documented in the literatures.[3 4] The mechanism of thrombosis in IDA may be due to anaemia-induced hypoxia leading to injury of endothelial cells in the retinochoroidal circulation, reactive thrombosis and coagulation dysregulation.[3 5 6] Examples of other life-threatening complications of IDA that were reported include strokes and pulmonary embolism.[7] Furthermore, as many as half of women who have IDA develop amenorrhea.[8]

In view of the COVID-19 pandemic, many countries have instituted lockdown measures such as the closure of food outlets or enforced stay-home restrictions.[9] This can lead to a change in eating behaviours with effects on nutrition and health.[10] The WHO recognised the challenges of COVID-19 containment measures on normal food-related practices and released guidance on food and nutrition to address the needs of individuals or families under periods of quarantine.[11]

In this case report, we present a young woman who developed CRVO and amenorrhea secondary to severe IDA attributed to a drastic change in dietary habits and reduction in iron intake during the COVID-19 pandemic.

## CASE PRESENTATION

A 23-year-old woman presented with a 1-week history of reduced left eye vision associated with amenorrhea for 4 months. She had normal menstrual cycles prior and no previous medical issues. When Singapore implemented the 'circuit breaker' or the equivalent of lockdown, there was a significant change in her diet that included red meat previously to mainly carbohydrates. Approximating her diet by using the concept of the healthy plate, her previous diet involved regularly eating out for steaks or mutton to mainly biscuits or potato-based food with mostly vegetables for her main meal after the lockdown along with dried fruits for snacks. Her meal portions were also reduced. Her weight dropped from 46 kg to 41 kg over the lockdown period. Relevant negatives included no previous miscarriages, venous thromboembolism, diabetes mellitus, hypertension or raised intraocular pressures. She also did not consume any traditional Chinese medicine, supplements or oral contraceptives.

On measurement of vitals, she was normotensive. Eye examination revealed unaided best corrected visual acuity (BCVA) of counting fingers on the affected left eye and 6/6 of the right eye. There was a grade 2 relative afferent pupillary defect in the left eye. Slit lamp examination of the anterior segments was completely normal.

Fundus examination of the left eye showed papilledema, intra-retinal haemorrhages of four quadrants, retinal veins tortuosity, cotton wool spots and associated cystoid macular oedema. There were no signs of neovascularisation. Fundus examination of the right eye was completely normal. The patient was diagnosed with a left eye CRVO and was treated with intravitreal bevacizumab 1.25 mg injection with good response. Fundal photos of both eyes 1 week post injection are shown in figure 1.

## INVESTIGATIONS

An extensive set of investigations was done on the patient. Profound microcytic hypochromic anaemia with haemoglobin (Hb) of 43 g/L (reference range 120–160 g/L) and mean corpuscular volume of 69.6 fL (reference 78–98 fL) was noted. Platelet level was normal at $288\times10^9$/L (range $140–440\times10^9$/L). The iron studies revealed IDA at iron levels <2 µmol/L (reference range 7.7–32 µmol/L) and high total iron binding capacity of 92 (reference range 39–60 µmol/L). Ferritin was normal at 2.8 (7.6–179 µg/L).



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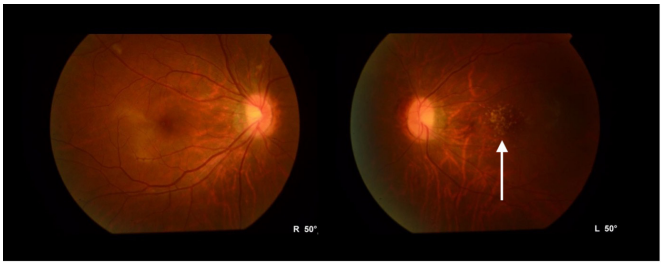


**Figure 1** Fundal photos of both eyes 1 week post Avastin injection. Arrow points to area of macula oedema that persisted 1 week post Avastin injection.

Oestradiol was low at <91.8 pmol/L and follicle stimulating hormone was inappropriately normal at 4.9 U/L, suggesting hypogonadotrophic hypogonadism.

A borderline low C3 of 0.85 (reference range 0.90–1.80 g/L) was also noted. All other laboratory parameters were normal including white blood cell count, renal panel, liver panel, quantitative beta-hCG, coagulation profile, thrombophilia screen, antinuclear antibodies, anti-double stranded DNA, anti-cardiolipin, lupus anticoagulant, thyroid function, prolactin, vitamin B12 and folate.

## DIFFERENTIAL DIAGNOSIS

The severe IDA was largely attributed to the lack of iron intake through her sudden change in dietary habits which happened over the period of lockdown. She did not have any symptoms to suggest blood loss and there is no significant chronic disease. The weight loss and anaemia contributed to her functional hypothalamic amenorrhea.

## TREATMENT

The patient was treated with 2 units of red blood cell transfusion, intravenous iron supplementation of 1 g ferric carboxymaltose once and subsequently oral iron supplementation of ferrous gluconate (250 mg ferrous gluconate per capsule) two capsules daily for 2 months. She was also given dietary advice on increasing iron in her diet by consuming more red meat.

## OUTCOME AND FOLLOW-UP

One month after iron replacement, the patient's vision improved. Repeat examination of the affected left eye revealed unaided BCVA of 6/15. Fundus examination of the left eye showed near full resolution of the central retina oedema. There were no signs of neovascularisation of the left eye. Right eye fundus examination was normal. A repeat dose of bevacizumab was given and her Hb improved to 130 g/L. Her diet currently includes more red meat compared with before.

## DISCUSSION

CRVO and amenorrhea contributed by IDA were reported in the literature before but this was the first case that was precipitated by COVID-19 related movement restrictions.[3 4] Disruption to diet and hence health is common when countries institute COVID-19 lockdown measures.[10] There are literatures that revealed that lockdown resulted in people purchasing more chips/snacks.[12–15] A scoping review by Bennett *et al* succinctly summarised the impact of a COVID-19 lockdown on changes in dietary habit in various populations.[16] One of the few papers in Asia by Husain *et al* revealed that lockdown measures resulted in reduced purchases of red meat, supporting our hypotheses of a lockdown-induced iron deficiency in our patient in this case report.[17] However, this is the first case whereby the severity of diet changes results in vision impairment and IDA has been reported.

IDA affects 11%–15% of young women in Asia.[18] IDA can result from insufficient dietary intake or excess loss through bleeding.[19] Iron replacement is therefore appropriate in the setting of deficiency, however, it should be administered judiciously.[19] Many mechanisms were hypothesised to explain thrombosis in IDA including endothelial injury, reactive thrombosis and hypercoagulability.[3 5 6] Factors including diet and lifestyle have also been investigated.[20] Iron is important for metabolism and phototransduction of the retina.[21] RPE-65, an iron-containing protein expressed in the retinal pigment epithelium, is an enzyme required to catalyse the conversion of all-trans-retinyl ester to 11-cis-retinol, which is an essential step in the visual cycle.[21] RPE-65 is important for maintenance of photoreceptor excitability by phagocytosis of shed photoreceptor outer segments, allow rebuilding of light sensitive outer segment of photoreceptors.[22 23] Furthermore, majority of secondary amenorrhea was due to nutrition-related anaemia.[24]

As CRVO with amenorrhea is not a common diagnosis in the young adult population, a thorough investigation for an underlying systemic aetiology including other ocular ischaemic syndrome, hyperviscosity syndrome, severe anaemia and advanced hypertensive retinopathy should be conducted.[3 25] Changes in dietary patterns can be significant during the COVID-19 pandemic due to movement restrictions. This case report should prompt clinicians managing sudden onset CRVO and amenorrhea during the pandemic to consider diet-related IDA as a potential cause and initiate nutritional assessment and early iron supplementation. Judicious supplementation with iron along with dietary advice to consume more red meat restored the patient's haemoglobin levels to normal with improvement of vision. Her menstrual cycle had not yet recovered at the time of writing of this report due to low body weight. This case highlights the importance of adequate nutrition on health during this period of COVID-19 pandemic.

## Patient's perspective

I did not realise that diet restrictions can lead to this condition that affected my eyesight. I am relieved that my vision has almost recovered fully.

## Learning points

- Lockdown measures during the COVID-19 pandemic can have significant impact on dietary patterns and lead to malnutrition.
- Consider iron-deficiency anaemia in patients presenting with sudden onset of central retinal vein occlusion and amenorrhea.
- Nutritional evaluation and supplementation may be considered in patients with drastic dietary pattern changes during quarantine measures due to COVID-19 pandemic.

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