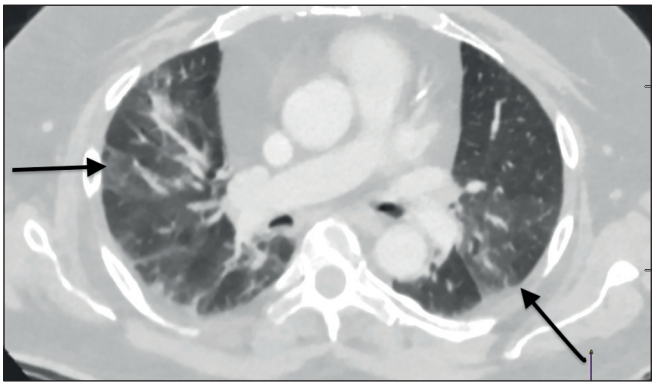
Figure 1.

Example of indeterminate findings on CT chest with ground glass opacification within basal aspects of both lower lobes (arrows).



The second patient was asymptomatic and RT-PCR negative. CT reported dependant lower GGO, equivocal for COVID-19. The patient proceeded to emergency laparotomy for intra-abdominal perforation. CT findings had no bearing on surgical management, however influenced bed management decisions.

The third case was a symptomatic patient with cough and fever, RT-PCR negative. CT reported GGO in the right upper lobe and multifocal consolidation in both lower lobes. The patient was managed conservatively for pancreatitis.

Additional CT chest screening had no impact on acute surgical management in our study. Due to increased radiation exposure, demand on radiology services and low diagnostic yield, BSTI/BSGAR advised that additional CT chest is no longer recommended[4]. Fortunately, we now have improved access to point-of-care testing e.g. LumiraDx SARS-CoV-2 Ag test which provides results within 20 minutes aiding timely surgical management[5].

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"WHY AM I SO YELLOW??" – LATE ONSET SEVERE HYPERBILIRUBINEMIA DUE TO CARBIMAZOLE THERAPY

Editor,

We present the case of a 38 year old male with late onset of severe hyperbilirubinemia 1 year after commencing carbimazole therapy. He had a history of hyperthyroidism, diagnosed in May 2019. His thyroid function tests (TFTs) were difficult to stabilize on carbimazole titration. Therefore, he was switched to block and replace treatment with carbimazole 40 mg and levothyroxine 100 micrograms daily after 3 months. TSH receptor antibodies were strongly positive in keeping with Graves' disease.

He presented to hospital in June 2020 with a 6 week history of jaundice, mild abdominal pain and feeling generally unwell. He had no prior history of liver disease and had a normal bilirubin in March 2020, with mildly cholestatic pattern of liver function tests. On admission, his bilirubin was 129 with a mixed cholestatic-hepatitic pattern of liver enzymes. Prothrombin time (PT) was raised at 15. Ultrasound imaging revealed normal liver structure with no biliary dilatation. Carbimazole was stopped and a full liver screen sent. He initially discharged himself against advice, however, he was re-admitted in July when his jaundice worsened and bilirubin had risen to 459 on repeat bloods with PT of 18.6. He did not have any other evidence of decompensated liver disease. MRCP showed no abnormalities within the biliary tree. Bilirubin continued to rise and liver biopsy was undertaken which revealed features of a mixed cholestatic-hepatitic liver injury, with the cholestatic injury significantly more prominent. It was considered most likely to represent a drug related liver injury. The patient had taken no other prescribed or over the counter medication and no illicit substances. Over time, liver function slowly improved and the jaundice resolved completely. Propylthiouracil was considered inappropriate for treatment given risk of hepatotoxicity and iodine was not practicable due to social circumstances. The patient went on to have a total thyroidectomy.

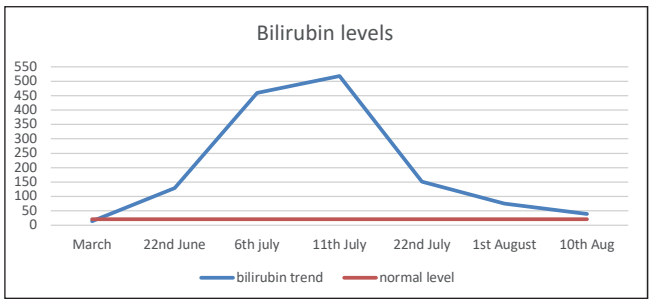

Fig 2: trend of bilirubin levels

Fig 1: summary of LFTs

	Normal reference ranges	March 2020	June 22nd 2020 (1st admission)	July 6th 2020 (community bloods and readmission)	July 11th 2020 (bilirubin peak)	July 22nd 2020	August 1st 2020	August 10th 2020
Bilirubin (umol/L)	<21	14	129	459	518	151	75	39
ALP (u/L)	30-130	187	266	305	267	267	138	144
AST (u/L)	<40	27	119	123	84	84	35	27
GGT (u/L)	10-71	100	110	Not report-able	Not reportable	52	97	74
ALT (u/L)	<41	35	138	130	88	81	29	16

Discussion:

Methimazole (active metabolite of carbimazole) has been associated with transient, asymptomatic elevations in serum aminotransferase levels, typically during the first 3 months after starting high dose, induction therapy.[1]

It can also cause a clinically apparent, idiosyncratic liver injury. Onset is usually within 2 to 12 weeks of starting therapy and typically causes a cholestatic or mixed pattern of enzyme elevations, without evidence of hepatic necrosis on liver biopsy.[2] Most patients recover on drug discontinuation. There are, however, occasional reports of severe and fatal cases. The proposed mechanism of carbimazole□induced cholestasis is not fully understood.[1]

This patient developed severe hyperbilirubinemia 1 year after starting treatment with carbimazole. His bilirubin level peaked at 518, significantly higher than reported levels in the literature to date. It then began to slowly settle over a period of 4 weeks. Although hepatotoxicity is a rare side effect of antithyroid medication, it can be a significant one. It is important to remember to consider it as a cause of jaundice, with the potential to occur many months after starting treatment. Patient awareness is very important and they should be counselled about the potential side effect and to consult a doctor if they notice jaundice developing. This patient waited for 6 weeks before seeking medical attention, without realising that his medication could be causing this problem.

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FACTORS ASSOCIATED WITH IMPROVED CLINICAL CONTROL IN A DIFFICULT-TO-TREAT PAEDIATRIC ASTHMA COHORT THROUGH THE COVID-19 PANDEMIC LOCKDOWN PERIOD

It is recognised that fewer children attended Emergency Departments (ED) with asthma exacerbations during the COVID-19 pandemic.[1,2] However, it is unclear why. The common triggers of asthma attacks include viral infections, high pollen counts and air pollution. It would seem likely that significant changes in one of more of these would impact on asthma control. There have been no reports, to our knowledge, examining asthma control and medication adherence in a paediatric difficult to treat (DTA) asthma cohort over this period, and comparing it with air pollution and respiratory viral data. The clinical course of, and external influences upon, the Northern Irish paediatric DTA cohort through the pandemic can inform this discussion. The UK

Table 1. Comparison of factors associated with asthma control for the Northern Irish paediatric DTA cohort between corresponding epochs in 2019 and 2020. Air pollution and pollen levels refer to daily levels measured in Belfast over the specified epoch

	1st Feb- 31st May 2019	1st Feb-31st May 2020	p-value
PM_{10} (μg/m³)	16·4 (10·6)	13 (5·6)	<0·01
$PM_{2.5}$ (μg/m³)	52·5 (24)	31·1 (12·9)	<0·01
SO_2 (μg/m³)	4·3 (2·2)	1·3 (0·6)	<0·01
NO_2 (μg/m³)	11 (4·9)	10·9 (7·8)	0·9
Plane tree pollen (grains/m³)	0·4 (1·5)	0·01 (0·1)	0·01
Hazel tree pollen (grains/m³)	1·1 (2·2)	0·4 (1)	<0·01
Ash tree pollen (grains/m³)	2·2 (4·6)	10 (23·3)	<0·01
Grass pollen (grains/m³)	0·4 (1·4)	2·3 (6·8)	0·04
Unscheduled care attendances /per patient*	0 (0,1)	0 (0,0)	0·01
ACT score (out of 25) *	17 (12,19)	20 (15,24)	<0·01
Number of courses of oral steroids/ per patient *	0 (0,1)	0(0,0)	0·01
Adherence (% collections of ICS prescriptions) *	100 (60,100)	100 (50,100)	0·6

Data are presented as Mean (SD) unless indicated.

* Median (IQR). Statistical tests used: Student t-tests and Wilcoxon rank-sum tests for non-parametric data. A p-value ≤0.05 indicated statistical significance.

ICS: Inhaled corticosteroids; ACT: Asthma Control Test; NO_2: Nitrogen dioxide; PM_{10}: Particulate matter less than 10 μm in diameter; $PM_{2.5}$: Particulate matter less than 2·5 μm in diameter; SO_2: Sulphur Dioxide.