BMJ Paediatrics Open

Early Recognition of PIMS-TS – A Case Series

Journal:	*BMJ Paediatrics Open*
Manuscript ID	bmjpo-2020-001011
Article Type:	Original research
Date Submitted by the Author:	30-Dec-2020
Complete List of Authors:	Mistry, Roshni; Whittington Health NHS Trust, Paediatrics Scanlon, Nicola; North Middlesex University Hospital Paediatrics, Paediatrics Hibberd, James; Andover Medical Centre, General Practice; The Northern Medical Centre, General Practice Fuller, Fionnghuala; North Middlesex University Hospital Paediatrics, Paediatrics
Keywords:	COVID-19, Virology

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Early Recognition of PIMS-TS – A Case Series

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Word count: 1187

Statements

Competing interests statement:
No competing interests

Funding Statement:
This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors

Contributorship Statement:

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Fionnghuala Fuller - Substantial contributions to drafting the work and final approval of the version to be published.

ABSTRACT

Introduction: PIMS-TS has emerged as a novel disease entity. Research has mainly focused on its management at tertiary care level. This article focuses on the symptoms and investigations at presentation.

Methods: Retrospective case note analysis of patients fulfilling PIMS-TS diagnostic criteria from March to May 2020 in a London district level university hospital.

Results: 11 cases were reviewed of which six (55%) had been seen in the hospital's Paediatric Emergency Department (PED) in the week prior to their final diagnosis. Initial presentations featured pyrexia and non-specific symptoms, especially vomiting. Raised CRP, lymphopenia and hyponatraemia were noted in the first presentations. Kawasaki like symptoms were underrepresented in all patients.

Interpretation: The results suggest that a significant proportion of children with early PIMS-TS will present to A&E with a non-specific febrile illness and abnormal blood results. Further research is needed to determine the most appropriate identification of these children.

What is known about this topic

Most children do not become unwell with COVID-19. A small proportion develop an exaggerated immune response leading to multi organ dysfunction called PIMS-TS.

Recent large studies have described the symptomology and the severity of this disease, with large numbers requiring intensive care treatment.

What this study adds

Research has mainly focused on PIMS-TS management at tertiary care level. This article focuses on the symptoms and investigations at presentation.

Results suggest children with early PIMS-TS can present with a non-specific febrile illness a few days before becoming unwell with more severe features.

Certain abnormal blood test results at this point may indicate early PIMS-TS. Further research is needed to ascertain the significance of these findings.

INTRODUCTION

Whilst most children experience only mild symptoms of Coronavirus disease 2019 (COVID 19),[1] a small group of children may suffer from severe disease associated with SARS-COV-2 infection. This is characterised by an exaggerated immune response leading to multi organ dysfunction and was first recognised in February 2020 in Italy as a cluster (29 patients) of 'severe Kawasaki like disease' at the epicentre of the COVID 19 epidemic.[2] This condition was termed Paediatric Inflammatory Multisystem Syndrome Temporally associated with Sars-CoV-2 (PIMS-TS).[3]

A systematic review published in September 2020 reported on 38 observational studies of 662 patients diagnosed with PIMS-TS. A high proportion of patients (71%) required admission to intensive care.[4] Most of these previous studies have focused on children's presentation at the time of admission to tertiary centres and the subsequent investigations and outcomes.

This paper looks at a cluster of 11 cases of PIMS-TS at a District level University Hospital in North London serving a population of approximately 300,000. It was noted by clinicians that a proportion of these patients had been reviewed in the Paediatric Emergency Department (PED) in the week prior to diagnosis. In addition to analysing clinical features at admission, this paper includes these initial presentations to explore if there are any early features of disease, which could enable earlier identification of these patients.

METHODOLOGY

Retrospective data was analysed for all children (aged 0-16 years) seen in North Middlesex University Hospital PED between March and May 2020 with an eventual discharge diagnosis of 'PIMS-TS' or who fulfilled the RCPCH case definition criteria for PIMS-TS.[3] If a patient presented more than once to PED during the data collection period, each presentation was included under the same case record.

All children requiring admission to hospital during this period were transferred to a tertiary centre due to temporary closure of all paediatric inpatient beds across the North Central London sector.

Data collected:

Data was collected based on the RCPCH PIMS-TS guideline[3] including patient demographics, presenting symptoms and the laboratory findings listed:

- Markers of widespread inflammatory response: C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white cell count, ferritin, fibrinogen, lactate dehydrogenase (LDH), D Dimer
- Markers of organ dysfunction: liver function tests (LFTs), renal function tests, cardiac enzymes, creatinine kinase
- Evidence of SARS-COV-2 infection: polymerase chain reaction (PCR) swab and serum serology results

RESULTS

Demographics

11 patients met the case definition criteria for inclusion. 5 (45.5%) were female and 6 (54.5%) were male. The mean age at presentation was 7.8 years (Range 18 months -13 years).

Initial presentations

Six patients were 're-presentations'. Of these, 5 had presented once before, and one had attended twice before. First presentation diagnoses for these patients were; COVID-19 infection, scarlet fever, migraine, viral upper respiratory tract infection, suspected bacterial sepsis and bacterial tonsillitis.

The mean time interval between first presentation and eventual admission was 2.7 days (Range 0 - 5 days).

The most common symptoms at first presentation were: fever (100%), vomiting (67%), headache (50%) and rash (50%) (Table 1).

Two patients were ambulated on IV antibiotics whilst the remaining four patients were reassured and discharged from PED with no follow up. One of these patients was given a course of oral antibiotics

All three patients who had bloods tested on first presentation had a raised CRP and lymphopenia. Two patients had hyponatraemia (67%) (Table 2).

Presentation at the time of admission to inpatient department

The most common presenting symptoms at admission were fever (100%), abdominal pain (73%), rash (55%), vomiting (55%) and difficulty in breathing (55%). Four patients (36%) were hypotensive on initial assessment (Table 1).

The pathology results showed that nearly all patients had a raised CRP (91%) and five patients were lymphopenic (45%). The mean CRP was markedly elevated (212 mg/L). ESR was measured in two patients and was raised in both. Eight patients were hyponatraemic (73%) (Table 2).

Fibrinogen and D Dimer results were elevated in the two cases where these were measured. Ferritin was measured in four cases and was elevated in all of these.

Pro-BNP was measured in one case and was significantly elevated.

Swab results for SARS-COV-2 PCR were negative in all 11 cases. Five patients tested positive for SARS-COV-2 antibody tests.

Table 1: Symptoms and observations on first presentation and admission

	At first presentation (n=6)	**On admission (n=11)**

Symptoms		
Vomiting	4 (67%)	6 (55%)
Headache	3 (50%)	3 (27%)
Rash	3 (50%)	6 (55%)
Abdominal pain	2 (33%)	8 (73%)
Sore throat	2 (33%)	2 (18%)
Confusion	2 (33%)	2 (18%)
Diarrhoea	2 (33%)	4 (36%)
Cervical Lymphadenopathy	1 (17%)	2 (18%)
Breathing difficulties	0 (0%)	6 (55%)
Cough	0 (0%)	2 (18%)
Conjunctivitis	0 (0%)	3 (27%)
Mucous membrane changes	0 (0%)	1 (9%)
Swollen hands and feet	0 (0%)	0 (0%)
Syncope	0 (0%)	0 (0%)
Observations		
Fever >38	6 (100%)	11(100%)
Fever >39	5 (83%)	9 (83%)
Fever >40	2 (33%)	4 (36%)
Hypotension	0 (0%)	4 (36%)
Tachycardia	4 (67%)	7 (64%)
Tachypnoea	4 (67%)	6 (55%)

Table 2: Lab results at first presentation and at time of admission

Lab results	**Reference ranges**	**Lab results on first presentation (n=3)**		**Lab results on admission (n=11)**	
		Mean	Range	Mean	Range
Haemoglobin (Hb)	115-155g/L	118	110-129	109.9	93-132
White cell count (WCC)	4.5-13.5 x10*9/L	7.51	4.73 - 10.07	11.7	2.02-31.16
Neutrophil count	1.5-8.0 x10*9/L	6.3	3.55-8.77	9.2	0.98-25.7
Lymphocyte count	1.5-7.0 x 10*9/L	0.73	0.63-0.83	1.7	0.45-3.3
Platelet count	150-450 x 10*9/L	194	180-230	230	93-299
C-Reactive protein (CRP)	0-20 mg/L	95	58-137	212.6	7.5 -328
Sodium	135-146	134.3	132-137	131.7	125-137

	mmol/L				
Erythrocyte sedimentation rate (ESR) (n=2)	0-10 mm/hr			68.2	17-120
Creatinine Kinase (n=3)	<190 U/L			209	47-442
Fibrinogen (n=2)	1.7-4.0 g/L			5.62	5.34-5.9
Ferritin (n=5)	17.2 -73.0 ug/L			816	335-1835
D Dimer (n=3)	0 – 312 ug/L			2155	630-3340
Troponin (n=4)	<34 ng/L			31	3-98
Lactate dehydrodenase (LDH) (n=0)	420-750 U/L			None measured	n/a
NT-pro brain natriuretic peptide (pro-BNP) (n=1)	29-206 pg/ml			4658	4658
SARS-COV-2 PCR positive swab (n=11)				0 (0%)	
SARS-COV-2 positive antibody test (n=9)				7 (78%)	

DISCUSSION

The results of this case series present some interesting comparisons with the current literature.

In common with the recent systematic review which showed that fever (100%), abdominal pain (73.7%) and vomiting (68.3%) were the most frequent symptoms at presentation, these symptoms were also significantly represented at both initial and admission presentation in this series. Again, in common with the systematic review it was found that most patients had a raised CRP, lymphopenia and hyponatraemia at initial presentation.[4]

There are, however, some significant differences. Early descriptions of PIMS-TS focused on its similarities to Kawasaki disease, with one study recording that 50% of patients had 'incomplete Kawasaki disease'.[2] The results of the systematic review appears to echo this with high rates of conjunctivitis (51.8%), oedema to extremities (19.3%) and lymphadenopathy (13.9%).[4] By contrast these symptoms were underrepresented in this case series with no such symptoms at first presentation and only some such as conjunctivitis (27%) and mucous membrane involvement (9%) appearing in a small number at admission.

Similarly, previous case reports have highlighted the severity of the illness with a UK based PICU series reporting shock (87%) as the second most common presenting feature after fever.[5] By contrast only 36% of patients in this series were hypotensive on admission. These differences in symptoms cannot be attributed to a milder form of PIMS-TS as many of this study's patients went on to receive cardio-respiratory support in intensive care.

It is likely that the differences discussed above are due to this series focusing on a period earlier in the disease's course. Given that over half of the patients in this series had been reviewed in hospital prior to the time of their eventual admission, this suggests that more consideration needs to be given to recognising this disease early before the more significant, and harmful, signs and symptoms develop.

Strengths and limitations

This study offers a unique perspective on PIMS-TS as there is minimal data available from other case reports of prior PED presentations for this patient group. Its strength is that we were able to follow every patient journey through from the first presentation to PED to referral to a tertiary centre.

The study is limited by the small case numbers involved making generalisation difficult.

Conclusion

The results of this case series suggest that children with early PIMS-TS can present to PED with a non-specific febrile illness a few days before they become unwell with the more severe later features. There is a suggestion that certain abnormal blood test results at this point may indicate early PIMS-TS. Further research is needed to ascertain the significance of these findings.

The authors support routine nationalised data collection for all cases of PIMS-TS. In addition to exploring optimal treatment options, a review of early signs, symptoms and investigation results will assist in answering the question of whether current accepted practices for investigation and follow up for patients with fever and nonspecific symptoms are adequate to ensure timely diagnosis of PIMS-TS.

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BMJ Paediatrics Open

Early Recognition of PIMS-TS: a single centre retrospective review

Journal:	*BMJ Paediatrics Open*
Manuscript ID	bmjpo-2020-001011.R1
Article Type:	Original research letter
Date Submitted by the Author:	02-Feb-2021
Complete List of Authors:	Mistry, Roshni; Whittington Health NHS Trust, Paediatrics Scanlon, Nicola; North Middlesex University Hospital Paediatrics, Paediatrics Hibberd, James; Andover Medical Centre, General Practice; The Northern Medical Centre, General Practice Fuller, Fionnghuala; North Middlesex University Hospital Paediatrics, Paediatrics
Keywords:	COVID-19, Virology

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Early Recognition of PIMS-TS: a single centre retrospective review

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Word count: 572

Statements

Competing interests statement:
No competing interests

Funding Statement:
This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors

Contributorship Statement:

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Fionnghuala Fuller - Substantial contributions to drafting the work and final approval of the version to be published.

Patient and public involvement statement:
It was not appropriate or possible to involve patients or the public in the design, or conduct, or reporting, or dissemination plans of our research

ABSTRACT

Research into PIMS-TS has focused on tertiary level management. This single centre retrospective review reports on symptoms and investigations at presentation of eleven patients with PIMS-TS admitted to a District General Hospital. Six patients presented in the week prior to their final diagnosis with pyrexia and non-specific symptoms. Raised CRP, lymphopenia and hyponatraemia were noted. Kawasaki like symptoms were underrepresented in all patients.

The results suggest that a proportion of children with early PIMS-TS present with a non-specific febrile illness and abnormal blood results. Further research is needed to determine the most appropriate identification and follow up of these children.

RESEARCH LETTER

Whilst most children experience only mild symptoms after contracting SARS-COV-2 infection,[1] a small number suffer from severe disease characterised by an exaggerated inflammatory response leading to multi organ dysfunction termed Paediatric Inflammatory Multisystem Syndrome Temporally associated with Sars-CoV-2 (PIMS-TS).[2] Most previous studies have focused on children's presentation and subsequent investigations at admission to tertiary centres. This review of eleven cases of PIMS-TS at a District University Hospital analyses clinical features at admission as well as previous presentations to explore if there are any early features of the disease.

Retrospective data was analysed for all children (aged 0-16 years) seen in North Middlesex University Hospital paediatric emergency department (PED) between March and May 2020 who fulfilled the RCPCH case definition criteria for PIMS-TS.[3] Data was collected based on the RCPCH guideline including patient demographics, presenting symptoms and relevant laboratory findings.[2]

Eleven patients met the criteria for inclusion. Five were female and six were male. The mean age at presentation was 7.8 years (Range: 18 months -13 years). Six children had been seen and discharged in the week prior to their subsequent diagnosis. Their initial diagnoses were: COVID-19 infection, scarlet fever, migraine, viral upper respiratory tract infection, suspected bacterial sepsis and bacterial tonsillitis. The mean time between first presentation and admission was 2.7 days (Range: 0 - 5 days). The most common symptoms at first presentation for these six patients were: fever (6 patients), vomiting (4 patients), headache (3 patients) and rash (3 patients) (Table 1). Two patients were ambulated on IV antibiotics whilst the remaining were discharged with no follow up. All three patients who had bloods tested on first presentation had a raised CRP (Range: 58-137 mg/L) and lymphopenia (Range: 0.63-0.83x10*9/L), two had hyponatraemia (Results: 132 and 134 mmol/L).

At admission the most common symptoms were fever (11 patients), abdominal pain (8 patients), rash (6 patients), vomiting (6 patients) and difficulty in breathing (6 patients) (Table 1). Ten patients had a raised CRP (Range: 7.5 -328 mg/L, Mean: 212 mg/L), five were

lymphopenic (Range: 0.45-3.3 10*9/L) and eight were hyponatraemic (Range: 125-137mmol/L). Fibrinogen, D Dimer, ferritin, pro-BNP and ESR were raised in all patients in which they were tested. Seven patients had positive SARS-COV-2 antibody tests.

Table 1: Symptoms and observations on first presentation and admission

	At first presentation (n=6)	**On admission (n=11)**
Symptoms		
Vomiting	4	6
Headache	3	3
Rash	3	6
Abdominal pain	2	8
Sore throat	2	2
Confusion	2	2
Diarrhoea	2	4
Cervical Lymphadenopathy	1	2
Breathing difficulties	0	6
Cough	0	2
Conjunctivitis	0	3
Mucous membrane changes	0	1
Observations		
Fever >38	6	11
Fever >39	5	9
Fever >40	2	4
Hypotension	0	4
Tachycardia	4	7
Tachypnoea	4	6

The results of this review present interesting comparisons with the current literature. A recent systematic review showed that fever (100%), abdominal pain (73.7%) and vomiting (68.3%) were the most frequent symptoms at presentation. These symptoms were also common in this cohort. Additionally, consistent with previous reviews most patients had a raised CRP, lymphopenia and hyponatraemia at presentation.[3]

In contrast with early descriptions of PIMS-TS which highlighted similarities to Kawasaki disease,[4] these symptoms were underrepresented in this review. One large case series reported shock (87%) as the second most common presenting feature in PIMS-TS,[5] however only four patients in this review were hypotensive on admission suggesting presentation earlier in the disease course.

The results of this review suggest that children with early PIMS-TS can present to PED with a non-specific febrile illness a few days before they become unwell with the more severe later features. Certain abnormal blood test results at this point may indicate early PIMS-TS, however this review is limited by the small case numbers making generalisation difficult. Further research is needed to ascertain the significance of these findings to determine whether current accepted practices for investigation and follow up for patients with fever and nonspecific symptoms are adequate to ensure timely diagnosis of PIMS-TS.

References:

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Methods: Retrospective case note analysis of eleven patients fulfillingwith PIMS-TS diagnostic criteria from Marchadmitted to May 2020 in a London district level university hospital.

Results: 11 cases were reviewed of which six (55%) had been seen in the hospital's Paediatric Emergency Department (PED)a District General Hospital. Six patients presented in the week prior to their final diagnosis. Initial presentations featured with pyrexia and non-specific symptoms, especially vomiting.. Raised CRP, lymphopenia and hyponatraemia were noted in the first presentations.. Kawasaki like symptoms were underrepresented in all patients.

Interpretation: The results suggest that a significant proportion of children with early PIMS-TS will present to A&E with a non-specific febrile illness and abnormal blood results. Further research is needed to determine the most appropriate identification and follow up of these children.

What is known about this topic

Most children do not become unwell with COVID-19. A small proportion develop an exaggerated immune response leading to multi organ dysfunction called PIMS-TS.

Recent large studies have described the symptomology and the severity of this disease, with large numbers requiring intensive care treatment.

What this study adds

Research has mainly focused on PIMS-TS management at tertiary care level. This article focuses on the symptoms and investigations at presentation.

Results suggest children with early PIMS-TS can present with a non-specific febrile illness a few days before becoming unwell with more severe features.

Certain abnormal blood test results at this point may indicate early PIMS-TS. Further research is needed to ascertain the significance of these findings.

~~INTRODUCTION~~

RESEARCH LETTER

Whilst most children experience only mild symptoms ~~of Coronavirus disease 2019 (COVID 19),~~[after contracting SARS-COV-2 infection,[1] a small ~~group of children may~~number suffer from severe disease ~~associated with SARS-COV-2 infection. This is~~ characterised by an exaggerated ~~immune~~inflammatory response leading to multi organ dysfunction ~~and was first recognised in February 2020 in Italy as a cluster (29 patients) of 'severe Kawasaki like disease' at the epicentre of the COVID 19 epidemic.[2] This condition was~~ termed Paediatric Inflammatory Multisystem Syndrome Temporally associated with Sars-CoV-2 (PIMS-TS).[~~3~~]

~~A systematic review published in September 2020 reported on 38 observational studies of 662 patients diagnosed with PIMS-TS. A high proportion of patients (71%) required admission to intensive care.~~[42] Most ~~of these~~ previous studies have focused on children's presentation ~~at the time of~~ and subsequent investigations at admission to tertiary centres ~~and the subsequent investigations and outcomes.~~

. This ~~paper looks at a cluster~~review of ~~11~~eleven cases of PIMS-TS at a District ~~level~~ University Hospital ~~in North London serving a population of approximately 300,000. It was noted by clinicians that a proportion of these patients had been reviewed in the Paediatric Emergency Department (PED) in the week prior to diagnosis. In addition to analysing~~analyses clinical features at admission~~, this paper includes these initial~~ as well as previous presentations to explore if there are any early features of the disease~~, which could enable earlier identification of these patients.~~

~~METHODOLOGY~~.

Retrospective data was analysed for all children (aged 0-16 years) seen in North Middlesex University Hospital paediatric emergency department (PED) between March and May 2020 ~~with an eventual discharge diagnosis of 'PIMS-TS' or~~ who fulfilled the RCPCH case definition criteria for PIMS-TS.[3] ~~If a~~Data was collected based on the RCPCH guideline including patient ~~presented more than once to PED during the data collection period, each presentation was included under the same case record.~~demographics, presenting symptoms and relevant laboratory findings.[2]

~~All children requiring admission to hospital during this period were transferred to a tertiary centre due to temporary closure of all paediatric inpatient beds across the North Central London sector.~~

~~Data collected:~~

~~Data was collected based on the RCPCH PIMS-TS guideline[3] including patient demographics, presenting symptoms and the laboratory findings listed:~~

- ~~Markers of widespread inflammatory response: C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), white cell count, ferritin, fibrinogen, lactate dehydrogenase (LDH), D Dimer~~

- ~~Markers of organ dysfunction: liver function tests (LFTs), renal function tests, cardiac enzymes, creatinine kinase~~
- ~~Evidence of SARS-COV-2 infection: polymerase chain reaction (PCR) swab and serum serology results~~

~~RESULTS~~

~~Demographics~~

~~11~~
Eleven patients met the ~~case definition~~ criteria for inclusion. ~~5 (45.5%)~~Five were female and ~~6 (54.5%)~~six were male. The mean age at presentation was 7.8 years (Range: 18 months -13 years).

~~Initial presentations~~

Six ~~patients were 're-presentations'. Of these, 5~~ children had ~~presented once before,~~been seen and ~~one had attended twice before. First presentation~~discharged in the week prior to their subsequent diagnosis. Their initial diagnoses ~~for these patients~~ were~~;~~: COVID-19 infection, scarlet fever, migraine, viral upper respiratory tract infection, suspected bacterial sepsis and bacterial tonsillitis.

The mean time ~~interval~~ between first presentation and ~~eventual~~ admission was 2.7 days (Range: 0 - 5 days).

The most common symptoms at first presentation for these six patients were: fever (~~100%),~~6 patients), vomiting (~~67%),~~4 patients), headache (~~50%)~~3 patients) and rash (~~50%)~~3 patients) (Table 1).

Two patients were ambulated on IV antibiotics whilst the remaining ~~four patients~~ were ~~reassured and~~ discharged ~~from PED~~ with no follow up. ~~One of these patients was given a course of oral antibiotics~~

All three patients who had bloods tested on first presentation had a raised CRP (Range: 58-137 mg/L) and lymphopenia~~. Two patients~~ (Range: 0.63-0.83x10*9/L), two had hyponatraemia (~~67%) (Table 2).~~Results: 132 and 134 mmol/L).

~~Presentation at the time of~~At admission ~~to inpatient department~~

~~The~~the most common ~~presenting~~ symptoms ~~at admission~~ were fever (~~100%),~~11 patients), abdominal pain (~~73%),~~8 patients), rash (~~55%),~~6 patients), vomiting (~~55%)~~6 patients) and difficulty in breathing (~~55%). Four~~6 patients ~~(36%) were hypotensive on initial assessment~~) (Table 1).

~~The pathology results showed that nearly all~~ Ten patients had a raised CRP (~~91%) and~~Range: 7.5 -328 mg/L, Mean: 212 mg/L), five ~~patients~~ were lymphopenic (~~45%). The mean CRP was markedly elevated (212 mg/L). ESR was measured in two patients and was raised in both. Eight patients~~Range: 0.45-3.3 10*9/L) and eight were hyponatraemic (~~73%) (Table 2).~~

Range: 125-137mmol/L). Fibrinogen ~~and D Dimer results were elevated in the two cases where these were measured. Ferritin was measured in four cases and was elevated in all of these.~~

~~Pro~~, D Dimer, ferritin, pro-BNP ~~was measured in one case~~ and ~~was significantly elevated.~~

~~Swab results for SARS-COV-2 PCR~~ESR were ~~negative~~raised in all ~~11 cases. Five~~ patients in which they were tested~~.~~ Seven patients had positive ~~for~~ SARS-COV-2 antibody tests.

Table 1: Symptoms and observations on first presentation and admission

	At first presentation (n=6)	**On admission (n=11)**
Symptoms		
Vomiting	4 ~~(67%)~~	6 ~~(55%)~~
Headache	3 ~~(50%)~~	3 ~~(27%)~~
Rash	3 ~~(50%)~~	6 ~~(55%)~~
Abdominal pain	2 ~~(33%)~~	8 ~~(73%)~~
Sore throat	2 ~~(33%)~~	2 ~~(18%)~~
Confusion	2 ~~(33%)~~	2 ~~(18%)~~
Diarrhoea	2 ~~(33%)~~	4 ~~(36%)~~
Cervical Lymphadenopathy	1 ~~(17%)~~	2 ~~(18%)~~
Breathing difficulties	0 ~~(0%)~~	6 ~~(55%)~~
Cough	0 ~~(0%)~~	2 ~~(18%)~~
Conjunctivitis	0 ~~(0%)~~	3 ~~(27%)~~
Mucous membrane changes	0 ~~(0%)~~	1 ~~(9%)~~
~~**Swollen hands and feet**~~	~~0 (0%)~~	~~0 (0%)~~
~~**Syncope**~~	~~0 (0%)~~	~~0 (0%)~~
Observations		
Fever >38	6 ~~(100%)~~	11~~(100%)~~
Fever >39	5 ~~(83%)~~	9 ~~(83%)~~
Fever >40	2 ~~(33%)~~	4 ~~(36%)~~
Hypotension	0 ~~(0%)~~	4 ~~(36%)~~
Tachycardia	4 ~~(67%)~~	7 ~~(64%)~~
Tachypnoea	4 ~~(67%)~~	6 ~~(55%)~~

~~Table 2: Lab results at first presentation and at time of admission~~

~~**Lab results**~~	~~**Reference ranges**~~	~~**Lab results on first presentation (n=3)**~~		~~**Lab results on admission (n=11)**~~	
		~~Mean~~	~~Range~~	~~Mean~~	~~Range~~
~~**Haemoglobin (Hb)**~~	~~115-155g/L~~	~~118~~	~~110-129~~	~~109.9~~	~~93-132~~

White cell count (WCC)	4.5-13.5 x10*9/L	7.51	4.73 - 10.07	11.7	2.02-31.16
Neutrophil count	1.5-8.0 x10*9/L	6.3	3.55-8.77	9.2	0.98-25.7
Lymphocyte count	1.5-7.0 x 10*9/L	0.73	0.63-0.83	1.7	0.45-3.3
Platelet count	150-450 x 10*9/L	194	180-230	230	93-299
C-Reactive protein (CRP)	0-20 mg/L	95	58-137	212.6	7.5 -328
Sodium	135-146 mmol/L	134.3	132-137	131.7	125-137
Erythrocyte sedimentation rate (ESR) (n=2)	0-10 mm/hr			68.2	17-120
Creatinine Kinase (n=3)	<190 U/L			209	47-442
Fibrinogen (n=2)	1.7-4.0 g/L			5.62	5.34-5.9
Ferritin (n=5)	17.2 -73.0 ug/L			816	335-1835
D Dimer (n=3)	0 – 312 ug/L			2155	630-3340
Troponin (n=4)	<34 ng/L			31	3-98
Lactate dehydrodenase (LDH) (n=0)	420-750 U/L			None measured	n/a
NT-pro brain natriuretic peptide (pro-BNP) (n=1)	29-206 pg/ml			4658	4658
SARS-COV-2 PCR positive swab (n=11)				0 (0%)	
SARS-COV-2 positive antibody test (n=9)				7 (78%)	

DISCUSSION

The results of this case seriesreview present some interesting comparisons with the current literature.

In common with theA recent systematic review which showed that fever (100%), abdominal pain (73.7%) and vomiting (68.3%) were the most frequent symptoms at presentation, these. These symptoms were also significantly represented at both initial and admission presentation common in this series. Again, in common cohort. Additionally, consistent with the systematic review it was found thatprevious reviews most patients had a raised CRP, lymphopenia and hyponatraemia at initial presentation.[43]

~~There are, however, some significant differences. Early~~ In contrast with early descriptions of PIMS-TS ~~focused on its~~ which highlighted similarities to Kawasaki disease~~, with one study recording that 50% of patients had 'incomplete Kawasaki disease'.[2] The results of the systematic review appears to echo this with high rates of conjunctivitis (51.8%), oedema to extremities (19.3%) and lymphadenopathy (13.9%).[4] By contrast~~ ,[4] these symptoms were underrepresented in this review. One large case series ~~with no such symptoms at first presentation and only some such as conjunctivitis (27%) and mucous membrane involvement (9%) appearing in a small number at admission.~~

~~Similarly, previous case reports have highlighted the severity of the illness with a UK based PICU series reporting~~reported shock (87%) as the second most common presenting feature ~~after fever.[~~in PIMS-TS,[5] ~~By contrast~~however only ~~36% of~~four patients in this ~~series~~review were hypotensive on admission~~. These differences in symptoms cannot be attributed to a milder form of PIMS-TS as many of this study's patients went on to receive cardio-respiratory support in intensive care.~~

~~It is likely that the differences discussed above are due to this series focusing on a period~~ suggesting presentation earlier in the ~~disease's course. Given that over half of the patients in this series had been reviewed in hospital prior to the time of their eventual admission, this suggests that more consideration needs to be given to recognising this~~ disease ~~early before the more significant, and harmful, signs and symptoms develop.~~ course.

~~Strengths and limitations~~

~~This study offers a unique perspective on PIMS-TS as there is minimal data available from other case reports of prior PED presentations for this patient group. Its strength is that we were able to follow every patient journey through from the first presentation to PED to referral to a tertiary centre.~~

~~The study is limited by the small case numbers involved making generalisation difficult.~~

~~Conclusion~~

The results of this ~~case series~~review suggest that children with early PIMS-TS can present to PED with a non-specific febrile illness a few days before they become unwell with the more severe later features. ~~There is a suggestion that certain~~Certain abnormal blood test results at this point may indicate early PIMS-TS~~.~~, however this review is limited by the small case numbers making generalisation difficult. Further research is needed to ascertain the significance of these findings~~.~~

~~The authors support routine nationalised data collection for all cases of PIMS-TS. In addition~~ to ~~exploring optimal treatment options, a review of early signs, symptoms and investigation results will assist in answering the question of~~determine whether current accepted practices for investigation and follow up for patients with fever and nonspecific symptoms are adequate to ensure timely diagnosis of PIMS-TS.

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