A study on cardiac evaluation in Multisystem Inflammatory Syndrome in Children (MIS-C) associated with SARS COV-2

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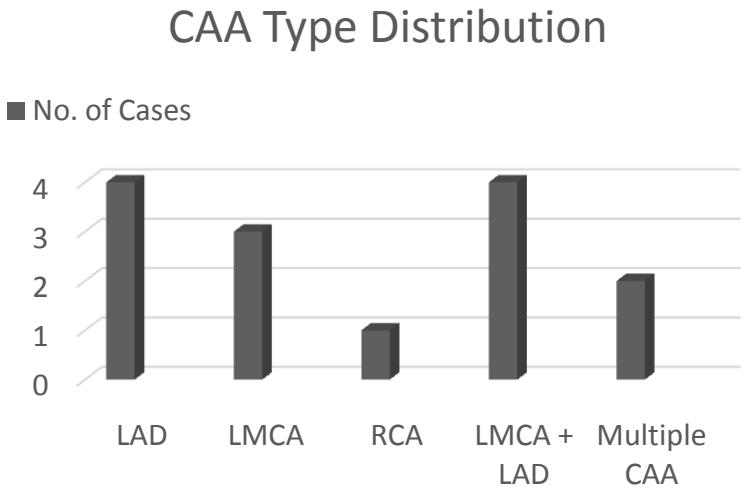
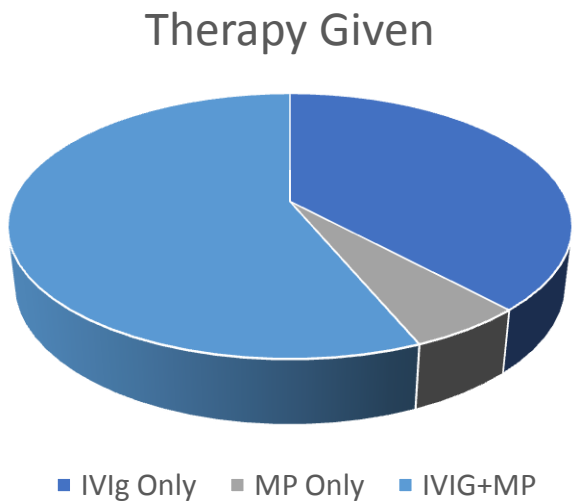
- **Introduction**: MISC is a multisystem disease but predominantly affects the heart causing sudden severe myocarditis, shock and coronary artery aneurysms(CAA).
- **Methods**: Patients satisfying WHO MIS-C criteria admitted at Institute of Child Health, Kolkata, India between July to December 2020 were included. All were evaluated clinically and by Echocardiography at admission and post treatment. Follow up echocardiography was done at 2 weeks, 6 weeks, 3 and 6 months. Treatment protocols and outcomes were noted down.
- **Results:**
  - 71 patients with a median age of 11 years (IQR 3 years) were admitted.
  - Intensive care (PICU) admission was needed by 45% and 29.5% required inotropic support.
  - Cardiac affection was present in 57.74% (n=41) mostly as myocarditis (disproportionate tachycardia, ECG and echocardiographic changes) of which 29.5% had low ejection fraction (EF 40 to 47%).
  - NT- Pro BNP and CRP was significantly higher amongst patients with cardiac affection; >935.7 pg/ml and > 99.55 mg/L at admission respectively might act as a guide as to the need for aggressive management.
  - 19 children (26.7 %) had CAA (Z score >+2) and Kawasaki Disease like manifestations. 4 had LAD dilatation (mean +3.18Z),3 LMCA dilatation (mean +2.51Z) and 4 had both (mean LMCA +3.57Z and LAD +3.31Z). 2 patients had multiple CAA involving LAD, RCA, LMCA. 1 had only RCA dilatation(+2.87Z).
  - 91.5% received IVIg, mostly at 2g/kg. Methylprednisolone (MP)only was given to 4 and 40 (56.3%) received pulse MP 10-30mg/kg/day x 3 to 5 days + IVIg.
  - EF improved by 48 to 72 hours of initiation of therapy. Patients presenting with shock, requiring inotropes, received MP + IVIg. On follow up, 89.5% patients with CAA's had regression by 6 weeks and rest over next 6 months.
- **Conclusion**: Acute myocarditis with or without CAA is the predominant cardiac affection in MISC. Early identification and aggressive therapy reverts it rapidly without significant residual lesions.





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Multisystem Inflammatory Syndrome in Children (MIS-C)- Our experience from Chandigarh, North India

Background:

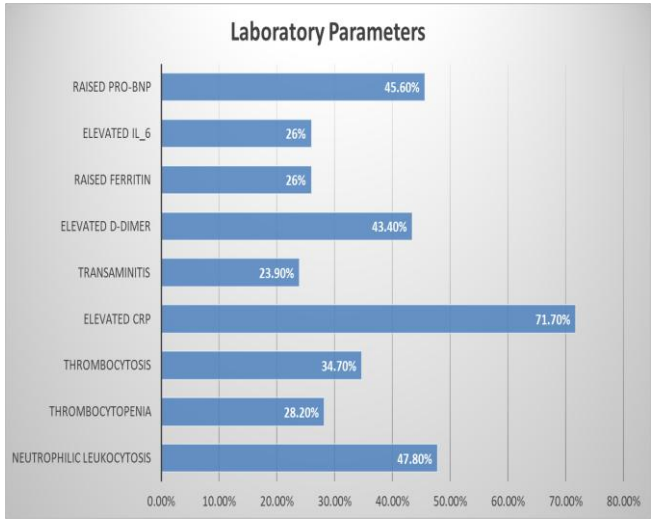
- **Multisystem inflammatory syndrome in children (MIS-C)** is a hyperinflammatory syndrome following severe acute respiratory syndrome coronavirus 2 (SARS Cov-2) infection.
- This study aims to analyze the epidemiological and clinical profile of MIS-C patients with emphasis on cardiovascular involvement.

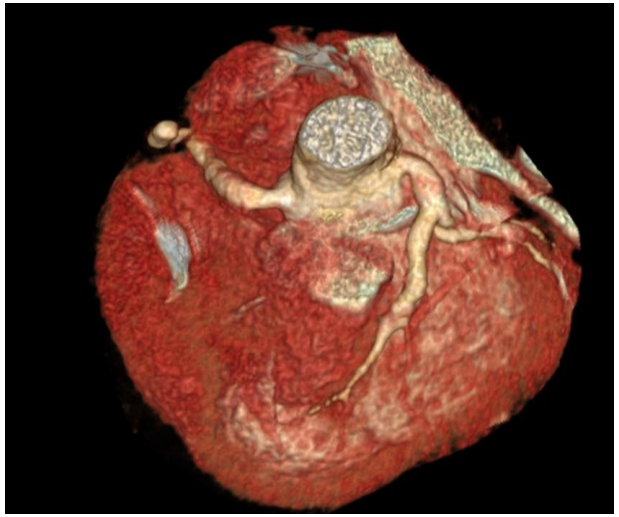
Methods:

- We analyzed **46 children** with MIS-C admitted to our unit from October, 2020 to October, 2021. **WHO MIS-C** criteria were used for diagnosis. We collated the demographic details, clinical features, laboratory parameters, treatment, and outcome of children with MIS-C with special emphasis on cardiac involvement.

Results:

- **Median age** of our cohort was **5 years (Range: 4 mo-15 years)**
- **Male: female ratio** of **2.8:1**
- **History of covid exposure** was present in **36.9%** and **73.9%** were positive for **SARS Cov-2 serology**
- **Predominant manifestations at presentation** were **fever (95.6%), rash (71.7%), eye changes (60.8%), mucosal changes (52.2%), gastrointestinal symptoms (vomiting/diarrhea) (58.7%) and shock (26%)**
- **PICU admission** was required in **28.3%** of the patients and **15.2%** needed **inotrope support**
- **Cardiac abnormalities** detected by **2D Echocardiography** were **low ejection fraction in 8.6% (4/46)** and **coronary artery dilatation in 10.8% (5/46)** of children
- **CT-angiography** was done in **5 patients (10.8%)** and it showed **pancoronary dilatation (LMCA, LAD and RCA) in 2 children (4.3%)**
- While **intravenous immunoglobulin (IVIg) alone** was used in **19.5%** of the patients, **only steroids** was used in **4.3%** of the patients. Both **IVIg and Steroids** were used in **71.7%** of the patients and **infliximab** was used in **4.3%**
- **One mortality** was reported in this cohort.





Pancoronary dilatation: 3-D reconstruction of CT angiography

Conclusion :

- **MIS-C is a multisystem hyperinflammatory syndrome** with significant cardiac involvement.
- Although 2D-echocardiography is useful in initial detection and follow-up of cardiac involvement, **CT-angiography** can be used as an important diagnostic tool for **better delineation of coronaries**.

Long term anticoagulation therapy in infantile Kawasaki disease with persistent giant coronary aneurysms

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Introduction

- Patients with giant aneurysms after Kawasaki disease (KD) are at increased risk of coronary artery thrombosis, stenosis and myocardial ischemia.
- Long-term systemic anticoagulation is recommended to prevent thrombotic complications[1].
- Anticoagulation in infants remains a challenge due to difficulty in individual dose adjustment and need for frequent monitoring of anticoagulation.

Case summary

- 36 days old male child presented with fever for 10 days and refusal to feed for 1 day
- Treated as late onset neonatal sepsis elsewhere with I.V. antibiotics with no improvement, hence referred
- Came to our center on 11th day of illness.
- On day 5 of hospital stay (day 16 of illness), the child was noted to have erythema on abdomen lips and tongue, periungual peeling of skin of hands and feet.

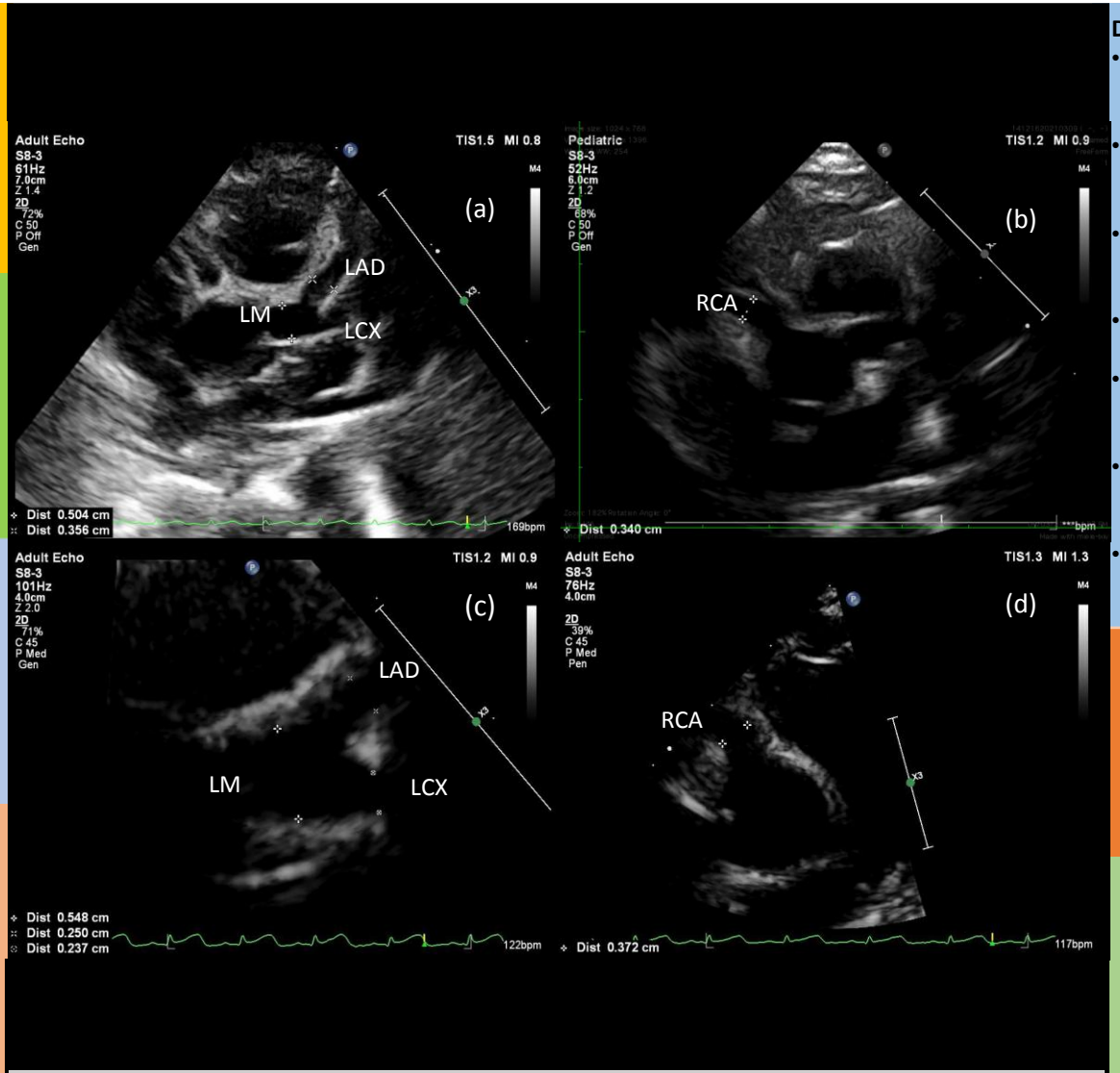
Investigations

- Hb 10.5g/dl, TLC 26550/μL, platelet count 6,65,000/μL, ESR 95, hsCRP 4.18mg/L, serum ferritin 686.8ng/ml, , LDH 207 IU/L , triglycerides 188mg/dl. Blood, CSF and urine cultures - sterile.
- Anti SARS-COV2 IgG antibody negative
- **Echocardiography revealed gaint aneuryms of left main(LM), left anterior descending(LAD), right coronary arteries(RCA)**, (LM 5.33mm, +13.5 Z, LAD proximal 3.8mm, +10.19 Z, RCA 3.85mm, +10.4 Z, LCX 2.5mm, +5.92 Z).

Course

- Antibiotics stopped, IVIG 2g/kg, ASA 50mg/kg/day and enoxaparin 1mg/kg twice daily started. 48 hours after the child became afebrile, ASA decreased to 5mg/kg/day, and continued on low dose ASA and LWMH (Enoxaparin) after discharge.
- During 4th month of follow up. the child had progression of coronary dimensions, hence he was readmitted and given a course of IVIG with high dose steroids, which resulted in regression of coronary aneurysms.
- There was no thrombotic or major bleeding complications during the follow up period.

Disclosures : None



Figures : Aneurysmal dilatation of (a)LM, LAD and LCX(b)RCA at presentation. Persistent dilatation of (c)LM, LAD, LCX and (d)RCA after 8 months.

Discussion

- Current recommendation for long term anticoagulation in KD with severe coronary involvement involves combination of aspirin and warfarin or LMWH[1]
- Problems associated with warfarin use in infants include need for regular INR monitoring and difficulty in maintaining therapeutic dose.[2]
- Plasma concentrations of many coagulation proteins including vitamin K dependent factors reach adult ranges only by 6 month of age[3]
- Late onset hemorrhagic disease of newborn (HDN) is a concern especially in infants less than 3 months.
- Warfarin maybe associated with more frequent incidence of major bleeding and greater risk of under- anticoagulation or over-anticoagulation. [2]
- LMWH is associated with comparable efficacy with that of warfarin with less frequency of major bleeding episodes but higher frequency of minor bleeding episodes. [2]
- Our patient had mild echymotic patches at the LWMH injection sites, but no other major/minor bleeding manifestations during follow up.

Conclusion

- LMWH appears to be a safe and viable alternative for long term anticoagulation in infants and smaller children where dosing adjustment and regular anticoagulation monitoring is difficult.

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A RETROSPECTIVE ANALYSIS OF THE NEED FOR METHYLPREDNISOLONE IN ADDITION TO IVIG FOR TREATING COVID-19 ASSOCIATED MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C).

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INTRODUCTION

- Multisystem inflammatory syndrome in children (MIS-C) has protean manifestations
- Cardiac involvement cause of morbidity
- Similarities with Kawasaki disease
- Evolving disease
- No universally accepted guidelines for treatment
- Management needs to be optimised

OBJECTIVES

- To retrospectively analyse the treatment to decide on need for methyprednisolne (MP) in addition to Intravenous Immunoglobulin (IvIg)

MATERIALS AND METHODS

- **Study period**: 6 months; July to December 2020
- **Study design**: Retrospective analysis of treatment data of patients with MISC admitted during the study period
- **Study location**: Institute of Child Health, Kolkata
- **Parameter used**: CRP and Ejection fraction (EF)

RESULTS

Incidence (n): 71

Median age: 11 yrs IQR 3 yrs

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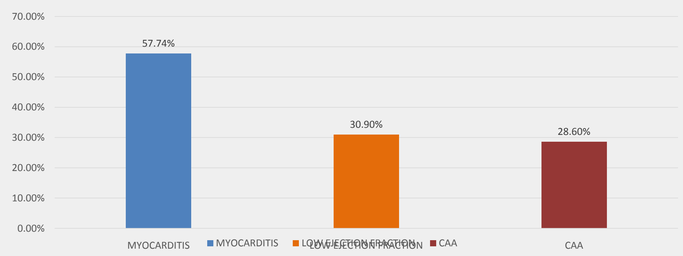
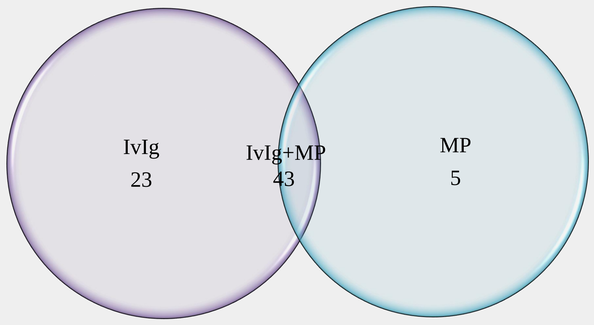
CARDIAC AFFECTION



TREATMENT



All patients responded to treatment
No mortality
45% required intensive care treatment
29.5% required inotropic support.
20% patients required respiratory support
4 children had to be intubated.
Following immunotherapy, inotropes tapered off over 48 to 72 hours
Normalization of EF by 5 to 7 days

RELATION BETWEEN MP PLUS IVIG WITH CRP AND EF

Logistic regression model

	P value	
CRP	>0.05	Not significant
EF	<0.05	Significant

CHI SQUARE TEST

	EF Normal (>55)	**EF Reduced (<55)**
MP+IvIg: NO	25	3
MP+ IvIg: YES	24	19

- P value <0.05, Significant

CONCLUONSI

- Patients with low EF will require MP in addition to IVIg; irrespective of CRP values.

DRAWBACKS

- Small study population
- Evolving nature of the disease

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Atypical Presentation of Multisystem Inflammatory Syndrome in Child

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Objective: We describe a child with Post COVID persistent fever, diarrhea and diffuse small bowel inflammation, suggesting an atypical presentation of MIS-C.

History: A nine-year-old boy presented with 2 months history of recurrent diarrhea, vomiting, pain abdomen, low grade fever, and weight loss of 6 kg. Past history was significant for having mild acute COVID 19 infection 2 months prior.

Clinical Features: He was investigated thoroughly for these symptoms in multiple centers. Hemoglobin was 9.7 g/dl, elevated ESR (37 mm) and thrombocytosis of 4.7 lakhs/cu.mm were noted. Ultrasonogram of abdomen showed small abdominal lymphadenopathy, Upper GI endoscopy showed fundal gastritis, duodenitis, and biopsy of D2 showed mild inflammation of the duodenum. colonoscopy was normal. CT abdomen showed small mesenteric lymph nodes. Mantoux test and TB Quantiferon Gold were negative.

On examination, he looked emaciated, and had few small cervical lymph nodes palpable. Other systemic examination was normal. He continued to have evening spikes of fever of 100 - 101^0 F during hospital stay. Blood cultures were sterile, Procalcitonin and 2D-Echo were normal. A whole-body PET CT done as a part of PUO work up showed diffuse thickening and enhancement of appendix, diffuse increased FDG uptake in entire small bowel loops with wall thickening and mucosal enhancement in duodenum, jejunal and ileum. Biopsy of ileum was recommended but the family refused. With TB workup negative, a possibility of atypical presentation of MIS-C was considered. He had a prolonged course as opposed to the acute presentation commonly seen in MIS-C and satisfied only 1 clinical criterion with Gastrointestinal symptoms. But other criteria of lab evidence of inflammation, infections ruled out and history of COVID 19 RT PCR positive supported the diagnosis.

Results: He was given a course of low dose corticosteroids for a month and responded well.

Discussion: In the setting of preceding COVID 19 infection, and prolonged inflammatory signs, infection ruled out by thorough workup, a post COVID inflammatory syndrome like MIS-C or Kawasaki syndrome were considered. There was no rash or mucosal involvement, 2D echo was normal and child was not acutely sick. We could not find any reports or literature of a chronic presentation of MIS-C but felt our case was an atypical presentation. Treatment options considered were a course of NSAIDs, a course of corticosteroids or IVIG. NSAIDs were not given as the child already had pain abdomen and we did not want to risk further GI upset. We felt the child was not acutely sick to try IVIG and so settled on a course of corticosteroids. A small bowel biopsy with TB cultures would have strengthened our basis for diagnosis and treatment but understandably, the parents were unwilling for another invasive procedure.

Conclusion: While classical Kawasaki and MIS- C are well known, atypical presentations should still be considered as part of the spectrum to help managing these cases. Further research is required for diagnosis and management , the duration of treatment and long-term prognosis or complications.

MISC : A comparative analysis of the 1ST &2ND waves

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INTRODUCTION

Multisystem Inflammatory Syndrome in Children(MIS-C)is a newly described hyperinflammatory syndrome occurring 2 to 8 weeks post Covid. The first MIS-C wave hit Bengal around July 2020 and lasted till January 2021. The 2nd wave started brewing in April and went on till July 2021.

AIM

The following study is a comparative analysis between the 2 waves.

METHODS

. Single centre study with patients who fulfilled the WHO MISC criteria. Clinical presentations, echocardiographic features, treatment protocols and outcomes were noted.

RESULTS

	2020 (n=75)	2021 (n=48)
Median Age	11 yrs	6.16 yrs (<2 yrs age= 8 patients)
History of COVID positivity	42.5%	68.75%
Rashes	86%	39.5%
Abdominal symptoms	70%	40%
Only febrile phenotype	3	13
Myocarditis	28.7%	39.5%
Coronary Artery Dilatations	29.5%	47.9%
PICU admission	45%	58.3%
Deaths	Nil	3 (1= MAS, 2= refractory myocarditis and hypotension)

TREATMENT GIVEN:	2020	2021
IVIG	38.7%	Nil
IVIG + steroids	56.3%	66.6 %
Only steroids	5 %	29.1%
Biologics	Nil	3 Infliximab

CONCLUSIONS

The 2nd wave was shortlasting but more intense affecting a higher number of younger children, with increase in only febrile phenotype and Kawasaki disease like presentations. Whereas majority of 1st wave children had abdominal symptoms and rashes, the numbers almost halved with the 2nd, with higher propensity of cardiac affection and need for PICU admission. Use of upfront steroids increased and only patients with myocarditis and Kawasaki like presentation received IVIG. Infliximab was used in 3 refractory cases and there were 3 deaths.

Kawasaki disease at a tertiary care center in South India – A Single Centre Experience Over 5 years

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Introduction

Kawasaki disease (KD) - most common cause of acquired heart disease in developed countries

Studies involving a large number of patients are sparse.

Objective

To study the profile of patients diagnosed with KD at a tertiary care center in South India.

Methods

- **Study period:** Feb 2017 to October 2021
- **Retrospective study-** all patients diagnosed with KD were included
- Clinical & laboratory profiles, including echocardiograms were reviewed
- Factors contributing to intravenous immunoglobulin (IVIg) refractoriness & the development of coronary artery abnormalities (CAA) were assessed

Comparison of clinical features and laboratory parameters in Kawasaki disease children with and without coronary artery abnormality

Clinical features	With CAA (n=14)	Without CAA (n=28)
n (%) Age <12 months	8/14 (57)	8/28 (28.5)
Gender		
Male	8/14 (53)	17/28 (60.7)
Female	6/14 (42.8)	11//28 (39.2)
Eye signs present	12/14 (85.7)	17/28 (60.7)
Mucosal changes present	14/14 (100)	24/28 (85.7)
Lymphadenopathy present	6/14 (42.8)	8/28 (28.5)
Extremity signs present	7/14 (50)	16/28 (57.1)
Rash present	13/14 (92.8)	24/28 (100)
Mean days of fever	10.4	9.4
CRP (mg/L)	63.9	67.2
ESR (mm at end of 1st hr)	74.9	60.8
Platelet counts (x 109/L)	6.8	5.1
TLC (×109/L)	15.4	14.3
Hemoglobin (g/L)	9.5	10.8

Conclusion

A significant proportion of infants with KD had cardiac involvement

Infants were more likely to have IVIg-resistant disease

Results

- Total sample size - **50 children**
- **42** received initial treatment at our centre
- **8 were referred** after the initial IVIg infusion for refractoriness to treatment &/or persistence of CAA (n=7) or pre-existing X-linked agammaglobulinemia (n=1). (excluded from the study)
- **Age range - 2 months to 11 years)**mean age was 3.1years)
- Most common clinical abnormality – **Mucosal involvement**
- Complete KD – 20 & Incomplete KD – 20
- 12/20 - incomplete KD cases were infants
- 20/50 children (40.8%) had CAA
- Most common artery involved: **LMCA** (n = 15), > **LAD** (n = 9) > **RCA** (n = 7)
- **Cardiac involvement - higher in infants** (8/16 had CAA vs 6/26)
- **Atypical features in infants with KD** - upper limb arterial thrombosis ,liver derangement and lower motor neuron facial palsy
- Refractory to treatment- 10 (20%) ; CAA was present in 8/10
- Five patients were treated with infliximab, three received methylprednisolone, while two received both infliximab and methylprednisolone.
- On follow- up, 3 patients had persistence of aneurysm.

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Profile of Multi System Inflammatory Syndrome in Children related to COVID19 - A Multi-centric study from South India

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Introduction:

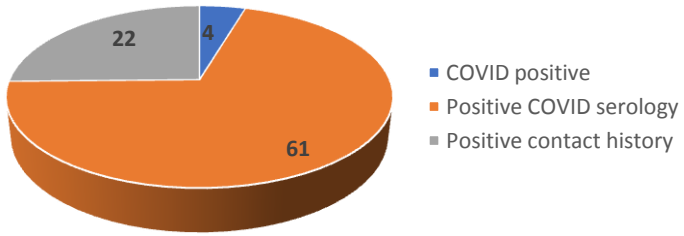
Multisystem Inflammatory Syndrome in Children (MIS-C) is a severe complication of SARS COV-2 infection associated with significant morbidity and can be fatal if left unrecognised.

Objective

To evaluate the clinical profile of children admitted with MIS-C associated with SARS-CoV2 infection

Method

- Retrospective multi-centric study carried out at **5 tertiary care centres** in South India
- MIS-C cases were diagnosed based on the **WHO criteria**
- ECHO was performed at admission, discharge, and 4-6 weeks of follow-up



Results

- A total of 81 children were diagnosed to have MIS-C
- Male: Female ratio-2.3:1

Clinical features	Current study N=81	Shobhavat et al [15] N= 21	Ahmed et al [18] N=622
Age in years (mean)	6.83 yrs	7yrs	9.3 yrs
Fever	100%	100%	100%
Conjunctival congestion	44(54.3%)	9(42%)	343(51.8)
Skin rash	44(54.3%)	7(33%)	372(56%)
Lymphadenopathy	20(24.6%)	-	92(13.8%)
GI symptoms	43(53%)	16(76%)	452(78%)
Shock	24(29.6%)	20(95%)	397(60%)
LV dysfunction (LVEF<50%)	22(27%)	9(43%)	-
Coronary dilatation	8(9.87%)	5(24%)	47(7.1%)
IVIG	65(80%)	11(52%)	504(76%)
Steroids	63(77%)	18(86%)	347(52.3%)
Discharge	81(100%)	18(86%)	651 (98.3%)

Conclusion

- **Largest Indian cohort** of patients with MIS-C
- Most children were treated with **IVIG & steroids (66.6%)** - all responded
- **Tocilizumab (1) & Anakinra (2)** was used in few patients
- Our study re-emphasizes the need for early diagnosis and timely referral in patients with MIS-C

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RARE CASE OF INFANTILE KAWASAKI DISEASE PRESENTING AS ASEPTIC MENINGITIS

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INTRODUCTION

Kawasaki disease (KD) is an acute vasculitis of infancy and early childhood. Incomplete and atypical forms of Kawasaki Disease are now being increasingly diagnosed and reported.[1] Infants <6 months of age with fever, rash and CSF pleocytosis presents a diagnostic dilemma because the clinical presentation in KD patients may initially resemble other infectious diseases, including bacterial or viral meningitis.[2] We hereby present a case of infantile KD with aseptic meningitis.

CASE DETAILS

3 month old male child presented with moderate grade fever spikes, loose stools since 4 days with maculopapular rash over cheeks since 2 days.
On examination child had cracked lips, bilateral conjunctival congestion, perianal rash, unilateral left cervical lymphadenopathy and hepatomegaly.
Child was started empirically on IV Ceftriaxone, IV Vancomycin with other symptomatic treatment.
Suspecting late onset sepsis, CRP, ESR sent were raised while lumbar puncture showed CSF pleocytosis (45 cells with 85% microglial cells).
Since high grade fever spikes persisted along with lymphadenopathy, erythema and cracking of lips with CSF pleocytosis clinical diagnosis of Kawasaki Disease with aseptic meningitis was made. 2D Echo showed dilated coronaries and Pro BNP sent was 1787 pg/ml confirming KD.

Child was given intravenous immunoglobulin (IVIG) @2g/kg and Aspirin (80mg/kg). Gradually fever spikes reduced, repeat inflammatory markers showed improving trend with normal coronary dimensions.

LABS

CRP	218.57 ng/ml
ESR	20
CSF	45 cells with 85% microglial cells ,
CSF culture	No growth
2D ECHO	Dilated Coronary arteries (Z scores >2.5)
PRO BNP	1787 pg/ml

DISCUSSION

The diagnosis of KD in this case was based on the following evidence:
Fever persisting for ≥ 5 days
- **Perineal area excoriation**
- **Polymorphous exanthem**
- **Changes in lips or oral cavity (fissured lips, strawberry tongue)**
- **Bilateral conjunctival injection**
- **Cervical lymphadenopathy (**unilateral, ≥ 1.5 cm)

KD with neurologic complications is uncommon. Aseptic meningitis often occurs in the acute stage, and the pathogenesis has not been fully elucidated. Possible mechanisms may involve systemic vasculitis due to the inflammatory response in pial vessels disease.
Similar 3 cases were reported by Muzaffer et al.[3] and a case by Bhardwaj P[4] was reported in India.

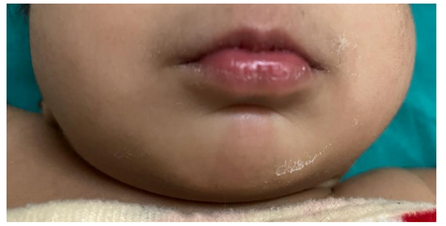

Fig 1- *Cracked lips*

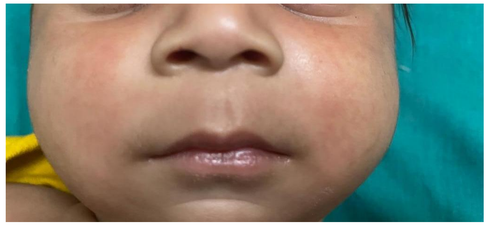

Fig 2- Maculopapular rash on the cheek

Fig 3- *Perianal excoriation*

CONCLUSION

As a conclusion, neurologic manifestations like aseptic meningitis may precede in KD. CSF pleocytosis is a common feature of acute KD and occurs in at least one-third of patients. The atypical form of KD seems to predict a higher risk of coronary dilatation; so, a high index of suspicion forts this diagnosis. Prompt recognition of the disease and early initiation of treatment with IVIG results in significant reduction in the occurrence of coronary artery abnormalities with better prognosis.

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Neutrophil NADPH oxidase activity in patients with Kawasaki disease

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Introduction

- Kawasaki disease (KD) is a systemic, medium vessel vasculitis
- Oxidative stress has an important role in pathology of KD as it triggers production of reactive oxygen species (ROS)
- NAD(P)H oxidase complex is the main source of ROS production
- The dihydro rhodamine assay (DHR) is done to quantify the functional status of NADPH oxidase system

Aim

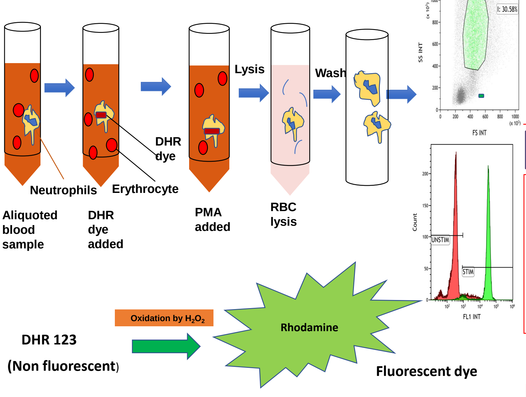
- To assess neutrophil NADPH oxidase activity in patients with Kawasaki disease

Methods

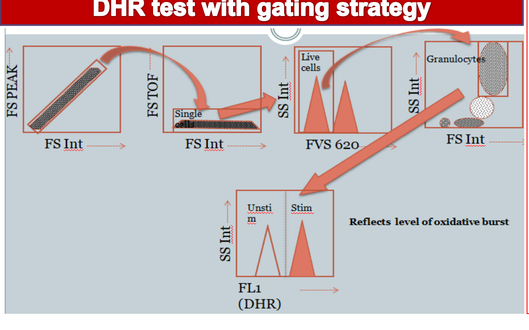
- This study was carried out to perform comparative analysis of NADPH oxidase function in KD patients with coronary artery aneurysms (CAAs) with healthy controls.
- A total of 14 KD patients were enrolled:
  Group1: Four patients diagnosed with KD (> 6 months-1.5 years; 2 with persistent, 2 with transient CAA) **Group 2**: Five patients diagnosed (>1.5 - 3 years; all with transient CAA)
  Group3:Five patients diagnosed(> 3 - 4.5 years; 2 with transient, 3 with persistent CAA) and 14 age matched healthy controls were enrolled
- DHR123 is oxidised to rhodamine by hydrogen peroxide generated during oxidative burst
- Rhodamine is a fluorescent dye and can be readily detected and measured on flow cytometer
- Auto-fluorescence of cells in FL1 channel was measured for un-stimulated cells after loading with DHR dye and fluorescence of dye after reduction due to ROS production upon phorbol myristate acetate stimulation was measured for stimulated cells
- Oxidative burst estimation was measured by calculating delta mean fluorescence intensity **(ΔMFI= MFI Stim-MFI Unstim)** and **Stimulation Index (S.I.) = MFI of Stained cells/MFI of unstained cells**

Results

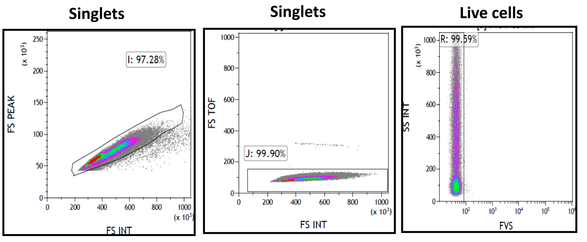
- The ΔMFI of patients was found to be higher (non-significant: Group 1 P=0.05; Group 2 P=0.30; Group 3 P=0.2) as compared to controls
- Inflammatory cell migration and infiltration to the arterial wall orchestrate ROS production leading to respiratory burst

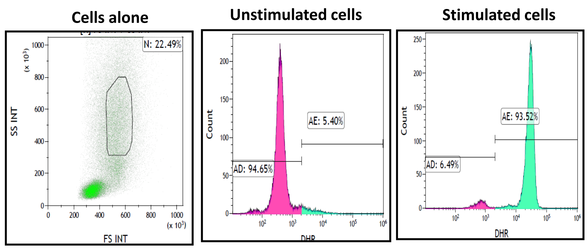


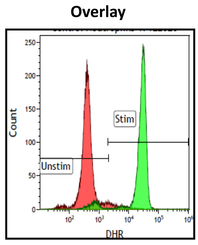
DHR test with gating strategy



Estimation of reactive oxygen species by DHR





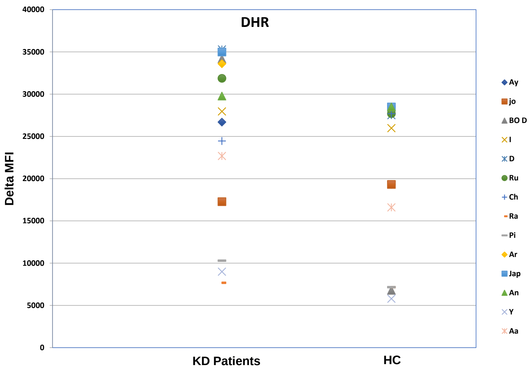


Name	MFI Unstimulated	MFI Stimulated	Δ MFI	Stimulation index	% Positivity
Control	404.99	27914.29	27509.3	68.92	93.52%

Calculation method: Oxidative Burst estimation

SI= MFI of Stained cells/MFI of unstained cells
ΔMFI= MFI Stim-MFI Unstim

Graph represents delta Mean fluorescence Intensity (ΔMFI; MFI Unstimulated cells - MFI (PMA) Stimulated cells



Discussion

- Oxidative stress plays an important role in the pathology of inflammation in KD
- Increased ROS production leads to endothelial dysfunction
- Chronic inflammatory response due to various risk factors causes vascular damage in arterial wall resulting in oxidative stress
- An excessive in vivo production of reactive oxygen species increases oxidative stress in the body that triggers vicious spiral of inflammatory reactions and production of reactive oxygen metabolites

Conclusion

- Oxidative stress has pathogenic role in functional changes of arterial wall
- ROS production was found to be enhanced in KD patients with CAA as compared to controls; however, this difference was not statistically significant probably due to small sample size

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Authors declare no conflict of interest

KAWASAKI DISEASE PHENOTYPE AND PHENOTYPIC SPECTRUM OF MULTISYSTEM IFLAMMATORY SYNDROME IN CHILDREN - SARS-COV2 ASSOCIATED IN A TERTIARY CARE HOSPITAL IN CENTRAL KARNATAKA

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INTRODUCTION

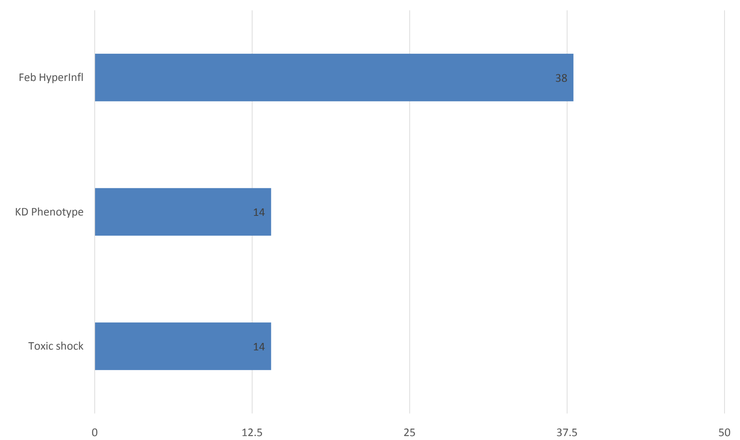
- Corona virus disease 2019 in children is usually mild but can cause inflammatory syndrome after SARS COV-2 infection.
- A phenotypic classification of the inflammatory syndrome helps in triaging, prevention of duplication of efforts and effective utilization of resources.
- Our objective is To profile the various clinical manifestation and phenotypically classify MIS-C as per WHO-IAP criteria including KD phenotype.

MATERIAL AND METHODS

- Descriptive observational study of children admitted with a
- diagnosis of MIS-C from the ages of 1month to 18 year in a tertiary hospital catering to central Karnataka between March 2021 and August 2021.
- Each patient underwent clinical and laboratory evaluation and were classified to MISC phenotypes.
- Inclusion criteria
  - all patients admitted to the hospital
  - 1 month to 18 years of age with a positive serology for SARS-CoV2
  - symptoms, signs, and laboratory markers in favor of a systemic hyperinflammatory condition
- Exclusion Criteria :
  - Children with tropical infections.
- Data was collected under the following headings -
  - Demographics
  - Clinical presentation
  - Co-morbidities and Co-infection
  - Level of inflammatory markers
  - Need for ventilator care
  - Duration of icu/hospital stay
- STATISTICAL ANALYSIS
- Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software.
- Categorical data was represented in the form of Frequencies and proportions.
  - Continuous data was represented as mean and standard deviation.

RESULTS

- Out of 400 children admitted to our tertiary care hospital, 80 were suspected of MISC and after exclusion criteria 64 children were proven to be MISC.
- Febrile inflammatory syndrome was the most common presentation (38cases-4.75%) followed by KD phenotypeand toxic shock syndrome.
- MISC can also present as organ dysfunctional symptoms and signs (6/64). Most of the children presented with history of fever from 2 nd to 12 th day with mean duration of 5days.
- 18 children received IVIG infusion and rest were treated with steroid and aspirin.
- Mean duration of hospital stay was 5 days. All the children are doing well in the short follow up.



DISCUSSION

- In this study, we have expressed that clinical presentation of post covid hyperinflammation is not restricted to MIS-C alone
- it has been observed that 38 children had only fever with positive covid antibody titres and raised inflammatory markers
- These children were identified as Febrile Hyper-inflammatory syndrome and were given symptomatic treatment.
- The illness was self limiting and did not warrant the use of steroids and anticoagulation.
- About 14 children had toxic shock phenotype. These children mainly presented with fever, rash and multi system involvement
- Kawasaki phenotype was identified in children presenting with fever, rash, lymphadenopathy and vomiting with leucocytosis and thrombocytosis and a raised ESR
- The main distinguishing characteristic was cardiac dysfunction(Myocarditis) and poor ejection fraction.
- 12 children were categorised into KD phenotype of which 4 were less than 1 year of age
- 6 children presented with other organ manifestation

CONCLUSION

Early phenotypic classification could help in management and in effective utilization of resources and finances. A high index of suspicion, early phenotypic classification and team dynamics helped in taking effective decisions and to differentiate between Kawasaki disease and Kawasaki like phenotype.

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KAWASAKI DISEASE AS A MANIFESTATION OF MULTISYSTEM INFLAMMATORY SYNDROME IN ASSOCIATION WITH SARS-COV2 INFECTION: A PROSPECTIVE STUDY FROM A TERTIARY CARE HOSPITAL OF NORTH-EAST INDIA

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INTRODUCTION

- SARS-CoV2 infection in children usually result in mild to moderate illness.
- Kawasaki Disease (KD) is the most common primary vasculitis in childhood[1].
- The Multisystem Inflammatory syndrome in Children (MIS-C) is a potentially serious complication associated with current or past infection with the virus.
- Sometimes children with MIS-C can present with KD.

OBJECTIVES

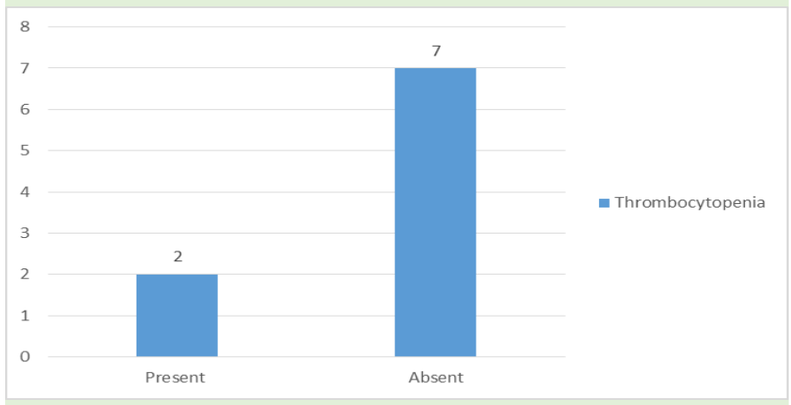
- To evaluate the clinical and laboratory profile of children admitted with Kawasaki disease as a manifestation of MIS-C over a one year period.

MATERIALS AND METHODS

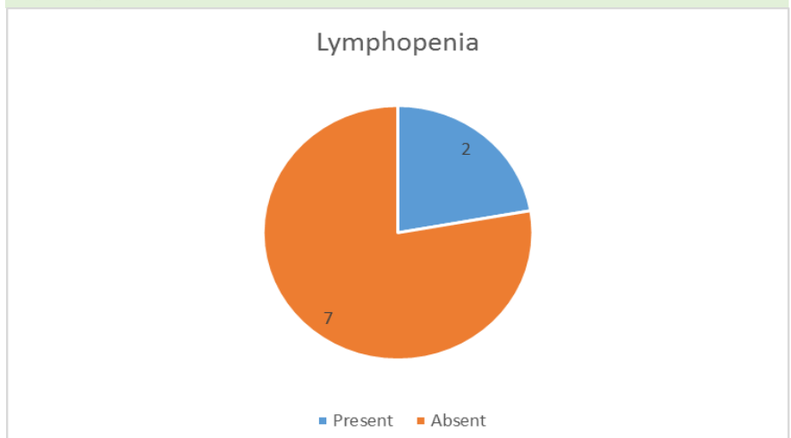
- **Study design:** Prospective study with limited follow-up.
- **Study duration:** 1 year from 1st September 2020 till 31st August 2021.
- **Study setting:** Pediatric Rheumatology Services of Department of Pediatrics, Gauhati Medical College and Hospital, Guwahati.
- **Inclusion criteria:** All patients with MIS-C who presented with features of KD.
- **Exclusion criteria**: Patients with MIS-C without the clinical features of KD.
- **Operational definitions:** The diagnosis of KD was based on the revised criteria developed by American Heart Association-2017.
- **Data collection and Analysis:** The data were collected in a pretested proforma on admission and on follow-up at the Pediatric Rheumatology and Immunodeficiency clinic and analyzed.

RESULTS AND OBSERVATIONS

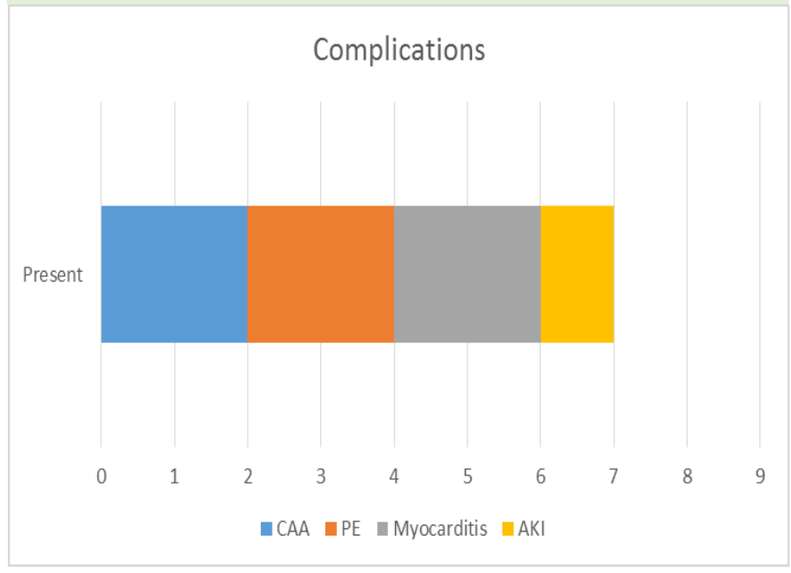
- A total of 9 patients were included in the study presented with features of KD. All patients had features of complete KD.
- The mean age at presentation was 9±2.4 years.
- Abdominal symptoms were present in 7 patients. Diarrhoea in 7 patients, acute abdominal pain in 6 patients and vomiting in 1 patient.
- The COVID-19 infection in the recent past was present in 1 patient.
- Thrombocytopenia was present in 2 cases.



- Lymphopenia was observed in 2 cases.



- The mean C reactive protein in the study group was 215.4±136.54 mg/dL.
- The d-dimer level in the study population was 5.12±4.71 µg/mL (normal range <0.5 µg/mL.
- The mean Erythrocyte Sedimentation Rate (ESR) in the study group was 66.33±39.81 mm AEFH.
- 1 patient presented with shock requiring ionotrope support .
- Complications included coronary artery abnormalities in 2 cases (bright coronary arteries 1 case, mild coronary abnormality 1 case), pericardial effusion in 2 cases, myocarditis in 2 cases and Acute kidney injury in 1 case.
- All cases were admitted in the intensive care unit.



- All patients responded dramatically to intravenous immunoglobulin (IVIG). The patients with CAA were additionally treated with oral glucocorticoids (2 mg/kg/day followed by tapering of doses and stopped after 3 weeks) and aspirin (3 mg/kg/day for 6 weeks).
- No residual CAA was seen in patients on follow-up.
- Favorable outcome was seen in all patients presenting with features of KD.

DISCUSSION

- The study suggests a causal link between covid-19 infection and KD, suggesting a post-viral immunological reaction.
- KD is typically a disease of young children <5 years old, whereas MIS-C has been reported in a wide age range with a median age of 6-11 years[2].
- Gastrointestinal symptoms such as diarrhea, vomiting, acute abdominal pain, which are predominant in children with MIS-C, are seen in most of our patients[3].
- Multisystem involvement was common in our study group.
- Lymphopenia, which correlates with severity and mortality of SARS-CoV2 infection was seen in 2 cases[4].
- Resistance to intravenous immunoglobulin and coronary artery abnormalities were less common in our study group.
- Very highs levels of CRP and high levels of d-dimer were seen in the study group.
- There was moderate elevations in ESR levels.

CONCLUSION

- KD in association with MIS-C can have similar presentation.
- However this subset of patients have predominant abdominal symptoms.
- Dramatic response to IVIG is also seen.
- Further studies are needed to explore the potential causality between SARS-CoV2 and KD.

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EPIDEMIOLOGY OF KAWASAKI DISEASE IN COVID TIMES

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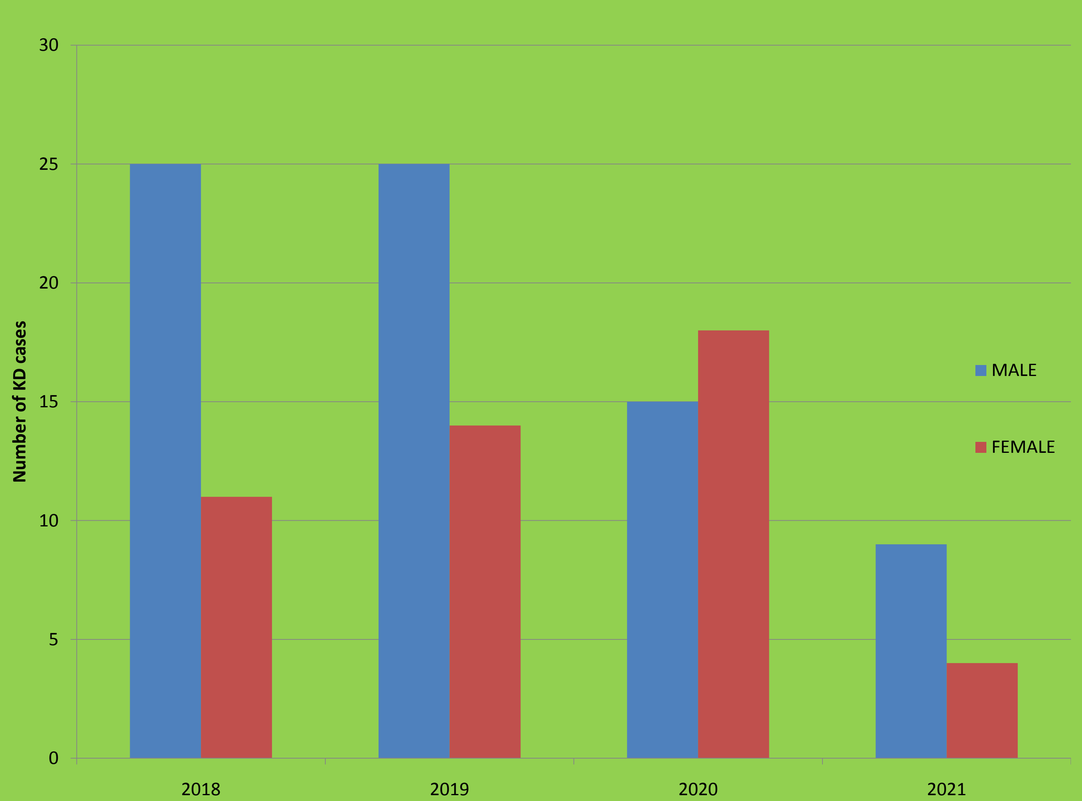
- **Background:** There is dearth of data on the epidemiology of Kawasaki Disease(KD) in India
- **Objective**: To estimate incidence of KD during the two pandemic years and compare it with the pre-pandemic years.
- **Methodology:** Data of KD patients admitted at the Institute of Child Health during the first and second wave of SARS-CoV2 were compared with data from the pre-COVID era
- **Results:**

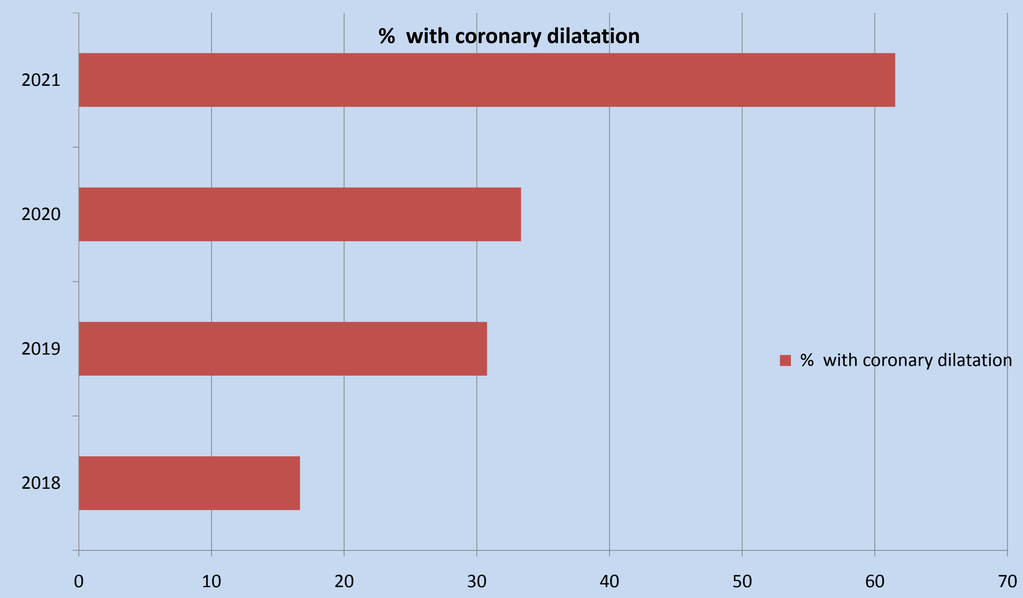
1. **The first wave(March 2020-December 2020**): 33 KD cases, 18 females and 15 males.
2. **The second wave(April 2021 - July 2021**): 13 KD cases, 4 females and 9 males.
3. In the pre-COVID era, the incidence of KD was:
   - **2018**: total cases 36, females 11 and males 25
   - **2019**: total cases 39, females 14 and males 25



4. There was a rising trend of KD every year with cases *doubling in number from 18 in 2009 to 39 in 2019*.

5. **First wave** had 33.33% cases and the **second wave** had 61.54% cases with *coronary dilatations* but no giant aneurysms (z score> +10) were seen during either waves. In comparison, in 2018 16.67% cases had coronary involvement with giant aneurysms in 2.78% and in 2019 30.77% cases had coronary involvement with giant aneurysms in 5.13%

5. **The first wave** had 75 cases of MISC, with *22 (29.33%) KD phenotypes*. **The second wave** had 48 cases of MISC, with *23 (47.9%) KD phenotype*. The second wave of MISC had a greater proportion of younger children (median age 6.6 years) with doubling of the KD phenotype.



- **Conclusion:**

1. Incidence of KD was similar to that of the preceding years, following the same upward trajectory despite the lockdown.
2. If the KD phenotype of MISC is taken into account, there was a 2 fold increase in the incidence of KD-like illnesses.

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