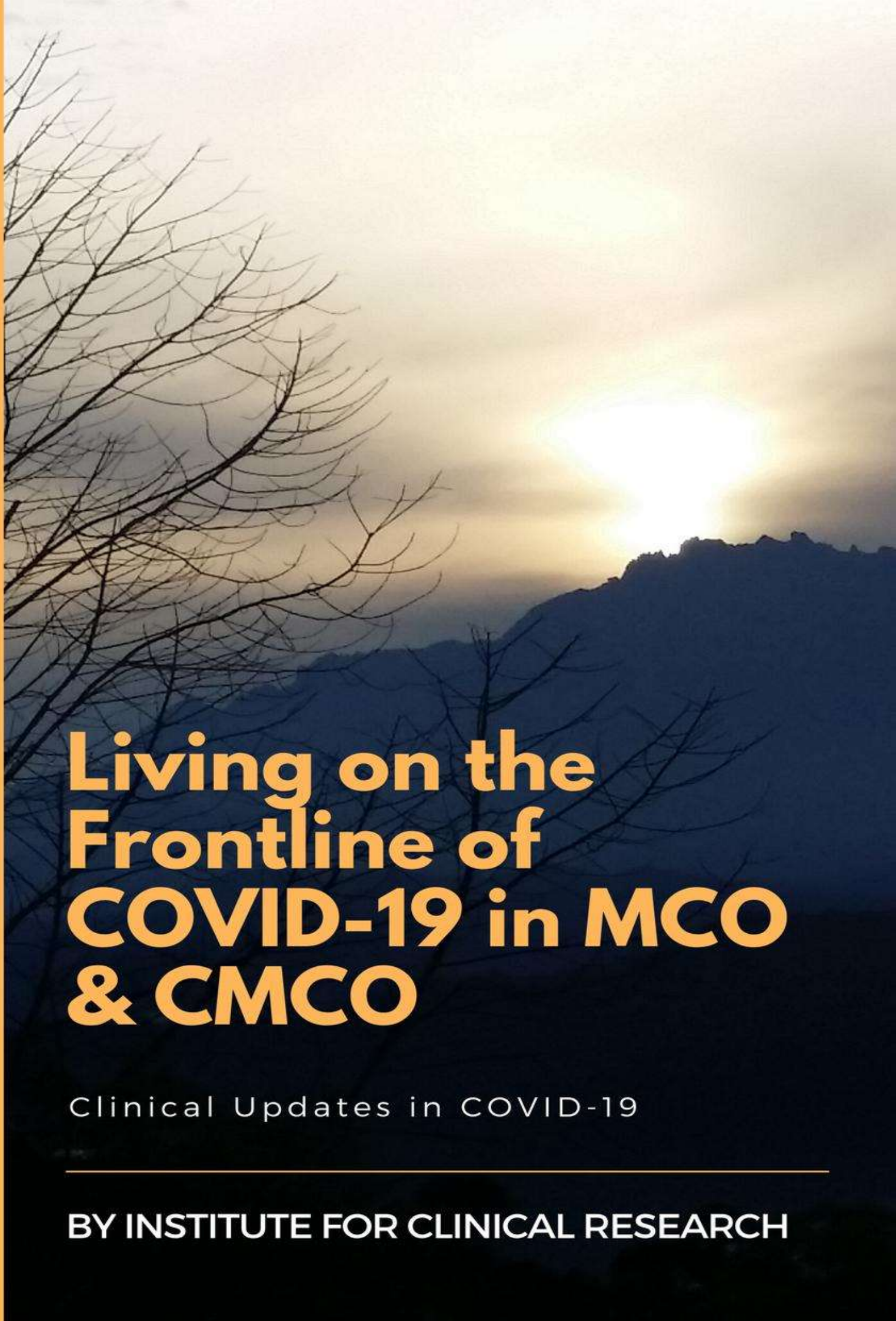

Living on the Frontline of COVID-19 in MCO & CMCO

Clinical Updates in COVID-19

BY INSTITUTE FOR CLINICAL RESEARCH

Living on the Frontline of COVID-19 in MCO And CMCO

Clinical Updates in COVID-19

Cheng Hoon Chew, Yan Yee Yip, Ming Tsuey Lim, Narul Aida Salleh, Syazatul Syakirin Sirol Aflah, Liang Choo Hung, Pei Jye Voon, Pik Pin Goh

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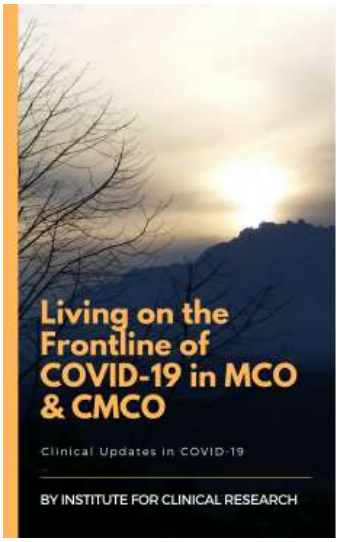
Front cover photo: Sunrise view of the Mount Kinabalu taken at 6:33 AM at Kokol Hill, Sabah on 16th August 2014 by Chew Cheng Hoon. Front cover design by Chew Cheng Hoon.

Written by Cheng Hoon Chew, Yan Yee Yip, Ming Tsuey Lim, Narul Aida Salleh, Syazatul Syakirin Sirol Aflah, Liang Choo Hung, Pei Jye Voon, Pik Pin Goh



Living on the Frontline of COVID-19 in MCO And CMCO

Disclaimer

- This transcript was prepared based on the Clinical Updates in COVID-19 live webinar session on 4/06/2020. The panellists for this webinar are Dr. Narul Aida Salleh, Dr. Syazatul Syakirin binti Sirol Aflah, Dr. Hung Liang Choo and Dr. Voon Pei Jye.

- The transcript was prepared by Ms.Yip Yan Yee, Mdm Lim Ming Tsuey and Dr. Chew Cheng Hoon from Institute for Clinical Research, NIH Malaysia.

- This is intended to share within healthcare professionals, not for the public.

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Q&A Session

1. Dr.Narul, recently, there is an article by Lancet (June 2020 Issue) which suggested that N95 masks might be a better option for all healthcare workers rather than a surgical mask?

2. Dr.Hung, since MIS-C has low platelets & reported false negative dengue serology in COVID-19 infection, how should we approach initially (eg. fluid management)?

3. Dr.Voon, to what extent did the practice of "new norm" affect the timeliness and quality of service deliveries?

Final Messages by Presenters:

Speakers' Brief Bio

“Management of ILI and COVID-19 in Health Clinic” by Dr.Narul Aida Salleh, Kuala Lumpur Health Clinic

Introduction

I'll be talking about the management of ILI (Influenza Like Illness) and COVID-19 in a health clinic setting. My name is Narul Aida Salleh. I'm a family medicine specialist, currently working in *Klinik Kesihatan* (Health Clinic) Kuala Lumpur.

References

- Guidelines COVID-19 Management In Malaysia No 05/2020 (5th Edition)

- *Garispanduan Pengendalian Influenza A (H1N1) Di Klinik Kesihatan. Cawangan Kesihatan Primer, BPKK, KKM. Pindaan 9*, 2009

- Clinical Practice Guidelines By The Infectious Diseases Society Of America: 2018 Update On Diagnosis, Treatment, Chemoprophylaxis, And Institutional Outbreak Management Of Seasonal Influenza

These are my references and what I plan to do in the next 15 minutes, I will try to outline the algorithm for management of ILI and PUI (Patient Under Investigation) in KK. I'll share some of our experiences managing ILI and PUI cases in our clinic.

Primary Care/ General practice

We basically provide community-based continuing comprehensive and preventive primary care. We are actually the point of first contact for the majority of people seeking healthcare service. So the unique thing about us in primary care is that we see patients with undifferentiated illnesses, and we often deal with problem complexes rather than with established diseases. Meaning, when the patients come to see us, they do not come with a diagnosis. In fact, they come with a range of problems and say, if a patient comes to see us with fever, it can be anything from dengue fever to just a simple viral infection or it can be leptospirosis, or influenza or even a common cold. Therefore, for us in Primary Care, the clinical judgment on the basis of the patient's disease presentation; disease severity and progression; the age of the patient; the underlying medical condition and the epidemiologic pattern of the infections in the community are important in helping decision-making on the patient's treatment and management, especially in those in the high-risk category.

Influenza-like Illness (ILI) & Severe Acute Respiratory Illness (SARI)

If the patient comes with fever and respiratory symptoms, we will see if they have **influenza like illness (ILI)**. If they fulfilled this definition: a history of high fever with temperature of 38 degrees or higher AND one or more of the following symptoms: cough, shortness of breath, body ache or sore throat.

If the disease is severe enough to require hospital admission and it occurs within the past 10 days, then the term **SARI or severe acute respiratory illnesses** is used.

Algorithm for Treatment of ILI in Adult Patients in Primary care - Before COVID-19 Pandemic

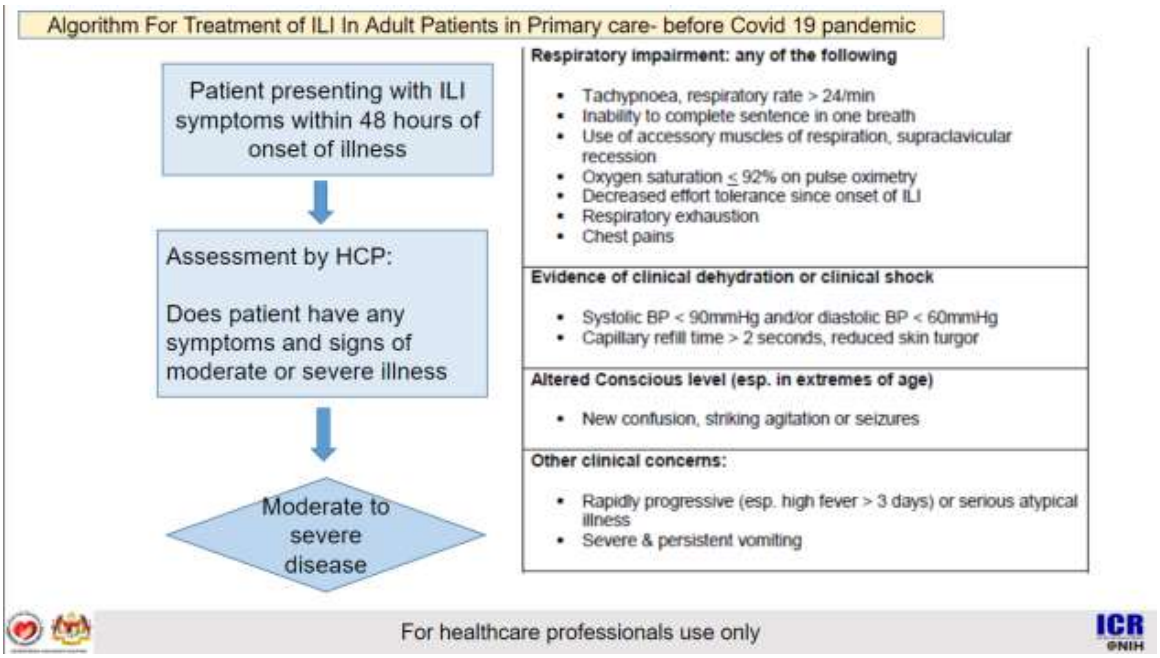

Diagram 1a: Algorithm for Treatment of ILI in Adult Patients in Primary care

So, if you see a patient presenting with ILI symptoms within 48 hours of onset of the illness, based on the guidelines, the healthcare provider should assess the patient to see whether the patient has any signs and symptoms of moderate or severe illness: i.e. we need to look whether they have any respiratory impairment, whether there is any evidence of clinical dehydration or clinical shock, altered conscious level or any other clinical concerns such as rapid progression of the disease or atypical illness or any severe or persistent vomiting.

We **should not forget about dengue** because our previous dengue mortality review had shown that in adults, around 19% of them presented with pharyngitis symptoms and in children, almost more than 30% were presented with fever and respiratory symptoms in the first presentation in dengue.

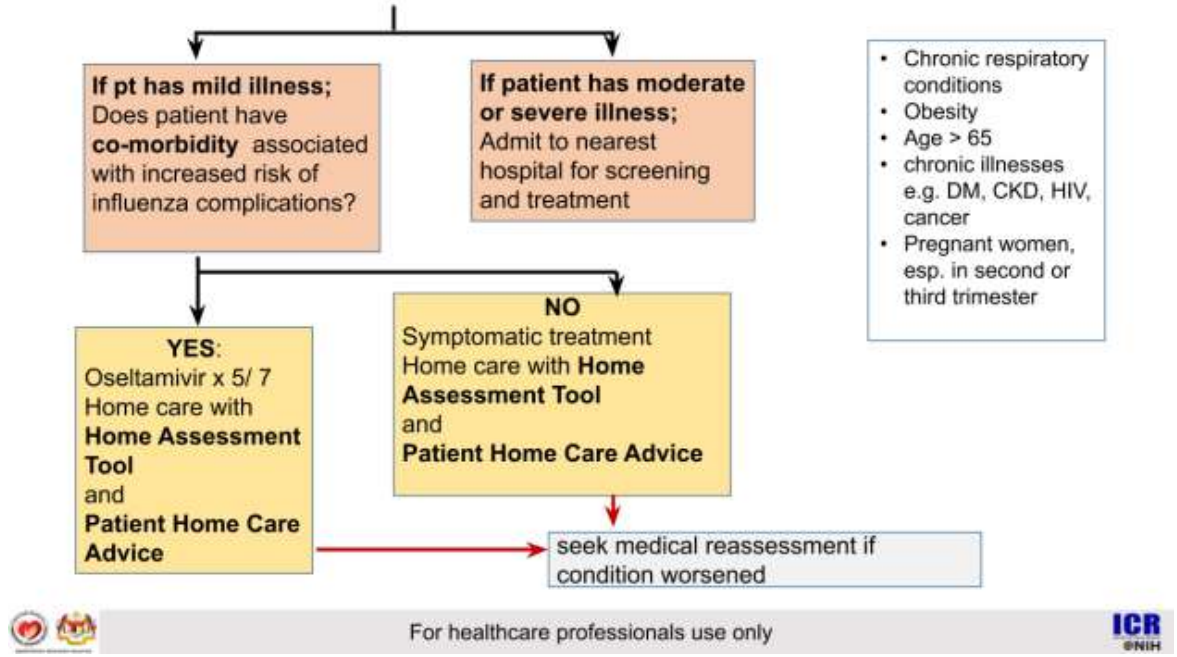

Diagram 1b: Algorithm for Treatment of ILI in Adult Patients in Primary care

After doing assessment, the health care providers should try to decide if patients have moderate or severe disease. If the doctor thinks that a patient has moderate or severe ILI, the patient should be admitted to the nearest hospital for SARI or severe acute respiratory infection. Otherwise, if the patient has mild Illness, the doctor has to assess for any comorbidity which can be associated with an increased risk of influenza complications. Comorbidity that we need to ask: if the patients have any chronic respiratory conditions, whether they are obese, whether there is any chronic diseases and whether they are pregnant.

If the patient has comorbidities and of mild illness and does not require hospital admission, and we made the diagnosis of influenza and if the patient comes to us within 48 hours, the patient should be treated with Tamiflu (oseltamivir) for five days. We should give them a home assessment tool for them to do assessment at home and home care advice. They need to be reminded to come back to see us if their conditions worsen. Otherwise, if the patients do not have any comorbidities, then symptomatic treatment will do. We will give them a home assessment tool and home care advice for them to return to see us if their conditions worsen.

Algorithm from the Infectious Disease Society of America

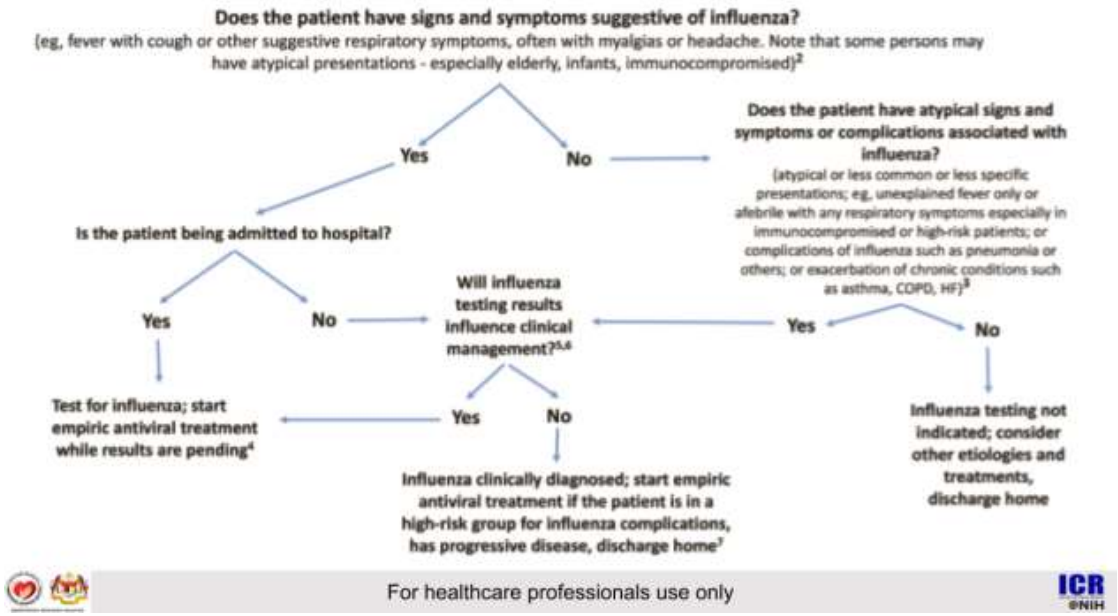

Diagram 2: Does the patient have signs and symptoms suggestive of influenza?

This is from the Infectious Disease Society of America (Diagram 2) and the guidelines are almost the same with ours.

The healthcare providers need to see whether the patient has any signs and symptoms of ILI. If yes, then the doctor needs to decide whether the patient requires hospital admission or not. If no hospital admission is required, then the doctor needs to decide whether the influenza testing will influence the clinical management. In our setting, unfortunately, we do not have any influenza testing in our KK. We just go by clinical judgment. If influenza is diagnosed clinically with high-risk for influenza complication, they also suggest empirical antiviral treatment.

How did we manage ILI before COVID-19 pandemic?

We put a triage counter at our registration counter. The triage staff are the paramedics: medical assistant or the nurses. They will ask the patients, the reasons for their visits. We will spot for symptoms of ILI. If the patients have fever, cough or shortness of breath, the triage staff will give masks to the patients. They will direct these patients to a designated area i.e. fever centre. We do not want them to mix with other patients in the clinic. In my clinic, we are fortunate because we have plenty of rooms. We have a special corner or area of the clinic where we designated it as a fever centre. These patients will go to this room, and they do not mix with the other patients, especially the NCD patients.

Management of ILI / PUI during the pandemic in health clinic setting (KK)

So how does the management of our ILI/PUI differ during this COVID-19 pandemic?

This is from our recent COVID-19 guidelines edition number 5: Management Of PUI As Outpatients. Based on the guidelines:

- patients who come to any health facilities should be screened for suspected COVID-19 at triage

- a special area should be set up for COVID-19 to which he/she can come directly be assessed in this designated area and these patients should be managed by a dedicated team.

Definition of PUI (Patient under Investigation)

PUI (patient under investigation) refers to any patients with acute respiratory infection (sudden onset of respiratory infection with at least one of these symptoms: shortness of breath, cough or sore throat) with or without fever

AND

there is a history of travelling to/reside in the foreign countries within 14 days before the onset of illness

OR

close contact in 14 days before illness onset with a confirmed case of COVID-19

OR

Attended an event associated with COVID-19 outbreak.

People under surveillance are those who get back from abroad, and they do not have any symptoms. But I guess for those who travel back from abroad, we do not have much problem because they would be quarantined at the hotels.

For close contacts, most of the time, the health inspectors will fetch them and give them home surveillance orders for them to be quarantined at home. Sometimes, we do see some close contacts who have not been traced by the health inspectors when they reached our site.

The guideline (Diagram 3) said, for patients under investigation, they should be triaged at the clinic entrance, and then they should be seen at the fever centre. The doctor should decide whether they meet criteria for hospital admission or not.

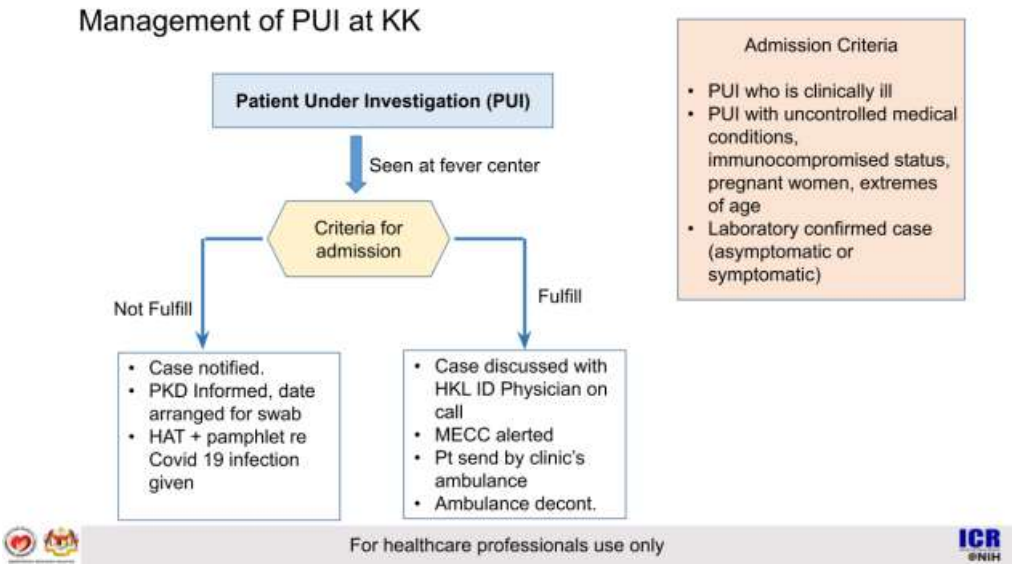

Diagram 3: Management of PUI in KK

Criteria for admission

What are the criteria for admission? Basically the criteria for admission are: PUI who is clinically ill, PUI with uncontrolled medical conditions or laboratory confirmed case (asymptomatic/symptomatic). Refer to the Diagram 3.

If the admission criteria are fulfilled, we will discuss with the HKL Infectious Disease (ID) physician on-call. If the ID physician agrees for the ward admission, then we will alert the MECC (Medical Emergency Coordinating Centre), which is the emergency department, HKL. The patient will be sent by our clinic's ambulance and the ambulance will then be decontaminated in the HKL hospital itself before it is back to the clinic.

Otherwise, if the hospital admission criteria is not fulfilled, we will notify the case to our PKD (District Health Office). The PPKP or health inspector will visit the patients at home. They were given home surveillance orders for them to be quarantined. They will arrange an appointment date for them to do nasal pharyngeal & oropharyngeal swabs, give home assessment tools and pamphlets about this infection.

Management of ILI during COVID-19 pandemic

What is important is the management of the movement of the ILI patient in the clinic. For patients presenting with ILI symptoms who are not PUI, how do we manage them during this pandemic?

For patients presenting with ILI symptoms, they are not allowed to enter our main building. They are triaged, and they will be seen by doctors in the fever centre. The doctors will assess the patient to see whether they are from the so-called "red zone areas". (Example: Kg Baru and Chow Kit are red zones for COVID-19 cases at that time) If we have patients from these areas, we are more alerted, especially if they sort of escaped from being screened by the PPKP.

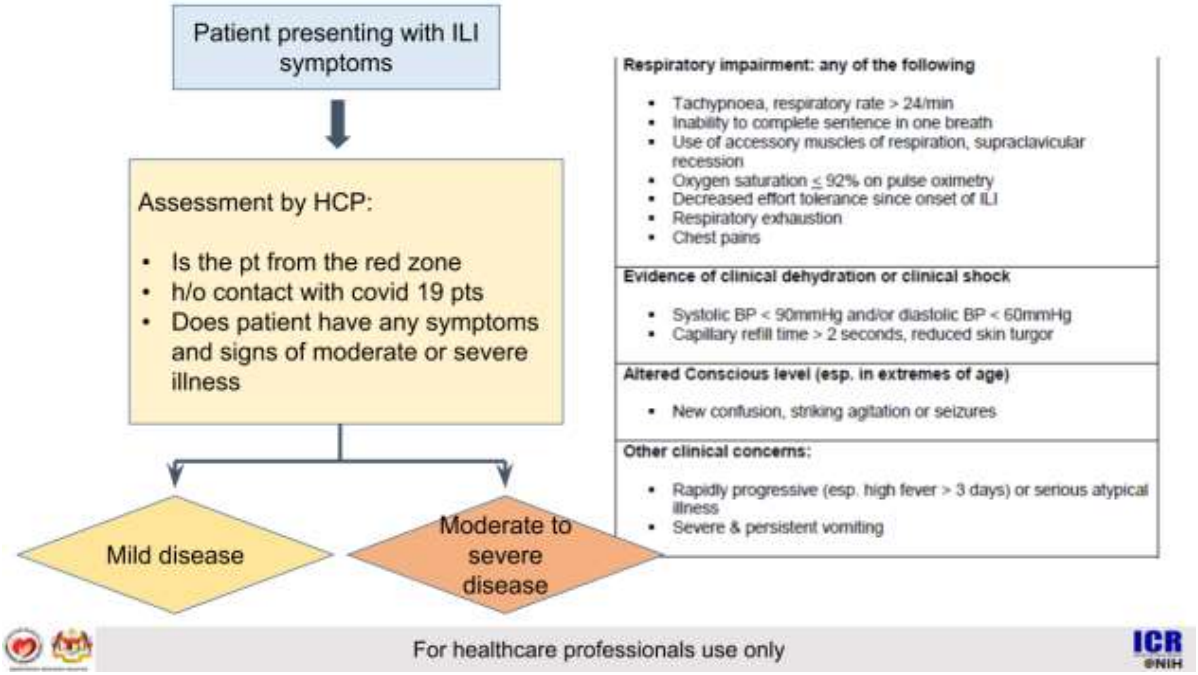

Diagram 4a: Management of ILI during COVID-19 pandemic

We would ask these ILI patients whether they have

- any history of contact with COVID-19 patients and
- any signs and symptoms of moderate or severe illness.

Then the doctor will decide whether they have mild or moderate to severe disease. So if they have moderate to severe disease and if the patients are suspected to be PUI, we will contact the ID physician on-call and patients will be sent to hospital for admission with a designated ambulance. But, if a patient does not have any history of contact with COVID-19 patients, that makes COVID-19 unlikely, but since he/she has moderate to severe disease, we will still send him/her for admission. However, we will admit the patient as SARI with COVID-19 unlikely.

For those with mild disease and suspected to be PUI, we will notify PKD. We will arrange a date for them to come back for the nasopharyngeal and oropharyngeal swab. We'll give them a home assessment tool and remind them to come back if the disease worsens. Otherwise, the PPKP will visit them in their home and serve them the home quarantine orders. If we suspect them of having influenza or URTI, we will manage them accordingly.

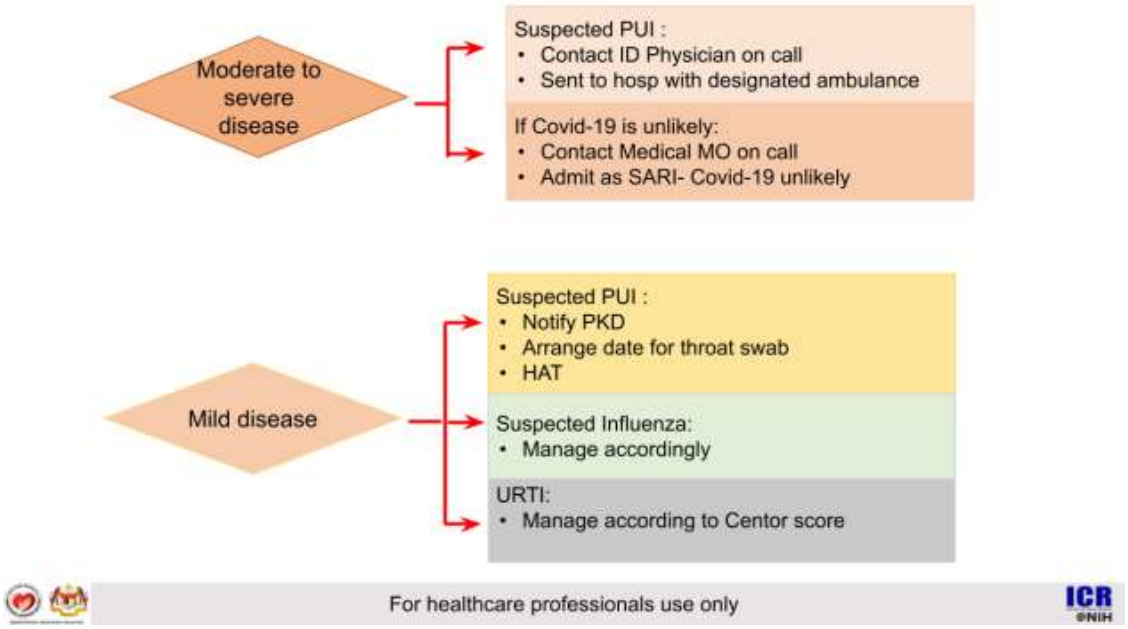

Diagram 4b: Management of ILI during COVID-19 pandemic

Movement of ILI patients

The movement of ILI patients are important. We do not want them to mix with other patients in the clinic. We had a triage counter outside the clinic entrance. The staff at the triage counter must wear at least three-ply surgical masks, gloves and apron, and we have asked them to do frequent hand rub before and after touching the patients. The triage staff will ask the patients the reasons for their visits and those with ILI symptoms will be given masks and will be directed to the fever centre.

Diagram 5a: Kuala Lumpur Health Clinic Fever Centre.

A) Fever Centre - The fever centre is at the tent beside the building

B) Registration - The registration of ILI patients is done in one of these tents.

C) Waiting Area - The orange colour tent is the waiting area for the patients.

D) Consultation - We have a consultation tent. The doctor will come out a clerking sheet template to make sure that the doctor does not miss any salient information.

Diagram 5b: Kuala Lumpur Health Clinic Fever Centre.

E) Doffing and donning personal protective equipment (PPE) Tent - Besides the consultation tents, we have donning and doffing tents for the doctors to put on and put off their PPE.

F) Mobile Toilet - Kuala Lumpur City Hall, DBKL are able to rent to us the mobile toilets. The patients as well as the staff do not have to go inside the main building if they need to use the toilet.

G) Decontamination of Fever Centre Tents - Every day, after 5 PM, the cleaning company, Global Company will decontaminate the tents.

Surveillance activity for the pandemic: Sentinel sampling

The main objective of the Sentinel sampling is to act as an early warning system for detection of local sporadic COVID-19 cases in the community. Initially the surveillance activities only involved 8 clinics but now it has been extended to 26 clinics. We do not do surveillance for all patients. Patients selected are those with acute respiratory symptoms who fulfil these criteria: sudden onset of respiratory infection, i.e. shortness of breath, cough or sore throat with or without fever and do not have any contact with confirmed COVID-19 cases. Those who fulfil these criteria will have nasopharyngeal and oropharyngeal swabs taken. Before this, we are asked to do 10 samples per week but now it has increased to 15 patients per week.

In our clinic, we will send the collected samples to the National Public Health Laboratory, MKAK in Sungai Buloh. We will fill up the MKAK forms, one copy sent to the lab (MKAK) and another copy to PKD. The specimens will be taken up in the VTM, the virus transport media and will be sent to MKAK on the same day. PKD will trace the results. Those who have positive results will be notified. The patient will be called, and we will arrange transportation for hospital admission either to HKL or hospital Sungai Buloh by our designated ambulance. State Health Department, JKN will analyze the surveillance data on a regular basis and check on the reports.

Outcome of sentinel sampling surveillance

What is the outcome of surveillance on sentinel sampling? The Director General (DG) of Health Malaysia, Datuk Dr Noor Hisham Abdullah's talked about the surveillance activities in his statement on 13 May 2020. He said although the number of sporadic cases is low, the ministry will continue its efforts to detect such cases early.

"*As of the 18th week of the epidemic, as many as 9,010 samples have been taken from ILI and SARI patients, out of which 81 cases or 0.9 percent were found to be COVID-19 positive*."

These are COVID-19 positive cases from the community who do not have any contact with confirmed COVID-19. The number of sporadic cases is not a lot, and in fact has been decreasing. However, it is important to detect these sporadic cases.

Acknowledgement

- Dr Rozita Zakaria. Consultant FMS, KK Presint 18, Putrajaya
- Dr Baizury Bashah, Consultant FMS, KKKL
- Dr Balamurugan a/l Irusan, Unit Infeksi, KKKL
- PKD Titiwangsa

Slide link: https://cutt.ly/kyCBkst

“The Scars of COVID-19” by Dr.Syazatul Syakirin Sirol Aflah, Respiratory Medicine Institute

Background

Beginning in December 2019, a cluster of unknown cause of pneumonia cluster was reported in Wuhan and in January 2020 a novel coronavirus, SARS-CoV-2 is being identified to be the causative organism. So, following that, it became a nightmare to the whole wide world where the outbreak was declared as the public health emergency of international concern and it was declared pandemic later on.

Coronavirus cases

How many cases are being reported? It is about 6.5 million whole wide world, with a death toll at about 385 thousands and about 3 million patients recovered from COVID-19. Malaysia had close to 8,000 cases confirmed COVID-19, and we have one of the highest recovery rates, about 6531 with 115 deaths.

What happened to the recovered patients?

So, what happened to all these recovered patients? What is their fate? Are they going back to their normal life? Are they actually up and about as before? So, there are a few speculations that have been around and in the news throughout the whole wide world saying that some patients who survived COVID-19 may suffer a lasting lung damage.

Article: Some patients who survive COVID-19 may suffer lung damage

There is a small study involving 12 patients in Hong Kong which discovered that the coronavirus patients who recovered are being left with damaged lungs, and they struggled to breathe when they walk. But this is just a small number to be looked at. Japan also said that these patients who survive will suffer severe health effects for years. In fact, Bloomberg also quoted that coronavirus survivors could suffer severe health effects for years. “Are patients left with poor lung function after COVID-19?” is still a question. This needs an answer.

Coronavirus Family: COVID-19, MERS & SARS

I am sharing a table of the coronavirus family which are the diseases of COVID-19, MERS and SARS. We could see the similarity in SARS-CoV-2 and SARS in which they actually shared the same receptor binding which is the Angiotensin Converting Enzyme 2. If you look at what happened to the lung in these 3 diseases, it showed that they have a similar pattern in which they were demonstrated on the chest computerized tomography (CT) scan. These three diseases will present with bilateral patchy shadows or ground glass opacity in the lungs.

	COVID-19	MERS	SARS
Epidemiology			
Time of origin	December 2019	June 2012	November 2002
Place of origin	Wuhan, China	Jeddah, Saudi Arabia	Fushan, China
Has travel history	Yes	Yes	Yes
Confirmed cases	84,305 (China)* 187,327 (Italy)* 843,937 (US)* 2,649,680 (global)*	2,494	8,096
Death cases	4,642 (5.50%, China)* 25,085 (13.39%, Italy)* 46,838 (5.54%, US)* 184,643 (6.96%, global)*	858 (34%)	744 (9.2%)
Healthcare worker cases	1,716 (2.03%, China)*	244 (9.8%)	1,870 (23.1%)
Spread	Animal to human, then human to human	Animal to human, then human to human	Animal to human, then human to human
Main transmission	Airborne, contact	Airborne, contact	Airborne, contact
Patient-to-healthcare-worker transmission	Yes	Yes	Yes
Months of epidemic period	N/A	>39	8
Infection control risk	High	High	High
Current status	Active	A few new cases	No new cases
Incubation period (d)	4–7	2–15	2–14
Infectivity, basic reproductive number	1.4–6.47	0.3–1.3	2.2–3.7
Virology			
Natural host	Bat	Bat	Bat
Intermediate host	Pangolins?	Camels	Civets
Human host	SARS-CoV-2	MERS-CoV	SARS-CoV
Lineage	Beta-CoV lineage B	Beta-CoV lineage C	Beta-CoV lineage B
Genome size	29.9 kb	30.1 kb	27.9 kb
Receptor	ACE2	DPP4	ACE2
Clinical features			
Principal symptoms	Fever, cough, fatigue, and shortness of breath	Fever, cough, fatigue, shortness of breath, and acute renal failure	Fever, cough, fatigue, and shortness of breath
Lab tests	Abnormal blood counts, abnormal coagulation, organ dysfunction, cytokine storm	Abnormal blood counts, abnormal coagulation, organ dysfunction, cytokine storm	Abnormal blood counts, abnormal coagulation, organ dysfunction, cytokine storm
CT scans	Bilateral patchy shadows or ground glass opacity in the lungs	Bilateral patchy shadows or ground glass opacity in the lungs	Bilateral patchy shadows or ground glass opacity in the lungs
Severe cases	Sepsis and septic shock	Sepsis and septic shock	Sepsis and septic shock
Clinical management			
Principal approach	Early supportive therapy and monitoring	Early supportive therapy and monitoring	Early supportive therapy and monitoring
Specific treatment	No	No	No

Table 1: Comparison between COVID-19, MERS and SARS

What were the evidences in the past?

What were the evidence in the past and how could we project what will happen to our recovered patients or COVID-19 survivors? We looked at SARS data because SARS and COVID-19 share the same receptors.

Study 1: Comparison between SARS patients with and those without evidence of fibrosis

A post SARS study done by Gregory et al. showed fibrosis was seen in 62% of the 24 symptomatic patients with SARS after treatment with symptoms of exertional shortness of breath and reduced exercise tolerance [1]. In this study, they divided patients into two groups: i) group 1 consists of patients with evidence of fibrosis on CT scan, n=15 and ii) group 2 is without evidence of fibrosis on CT scan, n=9. If you look at the profile patients that have evidence of fibrosis, the majority are men as compared to group 2, predominantly are female. The length of stay and the length of ICU admission are much longer in group 1, which consists of patients with lung fibrosis, and they received higher pulse steroid therapy during admission. They have even higher peak radiographic opacification and more abnormal segments on thin-section CT scan as compared to group 2 which without evidence of fibrosis. Besides discovering 62% of the patients having fibrosis, the patients also presented with symptoms of exertion of shortness of breath and reduced exercise tolerance.

Study 2: Long-term bone and lung consequences associated with hospital-acquired SARS

Another study is the 15 years prospective cohort study. They are actually looking at the long-term bone and lung consequences associated with hospital-acquired SARS [2]. However, I'm just focusing on the lung. Most of the cases will recover from the pulmonary interstitial damage and the functional decline caused by SARS, with a greater extent of recovery within two years after rehabilitation. So, you could dispute the speculation that had been made before for COVID-19 patients. But of course, we are not sure what we will face next for the COVID-19 recovered patients.

Study 3: Spirometric evaluation

The third study involved looking at spirometric evaluation. It showed that after six months, lung volume and spirometric measurements are normalized [3]. However, they have a low gas exchange or low carbon monoxide diffusion capacity in 12 months follow-up. No patients required supplemental oxygen at 12 months, but 6% of patients demonstrated desaturation with arterial oxygen saturation values below 88 percent during exercise.

Study 4: Exercise capacity and health status of SARS survivors

The fourth study has a small sample size, looking at the exercise capacity and health status of SARS survivors [4]. It showed that at the sixth month, their exercise capacity is lower compared to the normal population. There was a significant impairment in surface area for gas exchange was noted in 15.5% of survivors.

Study 5: COVID-19 illness in native and immunosuppressed states

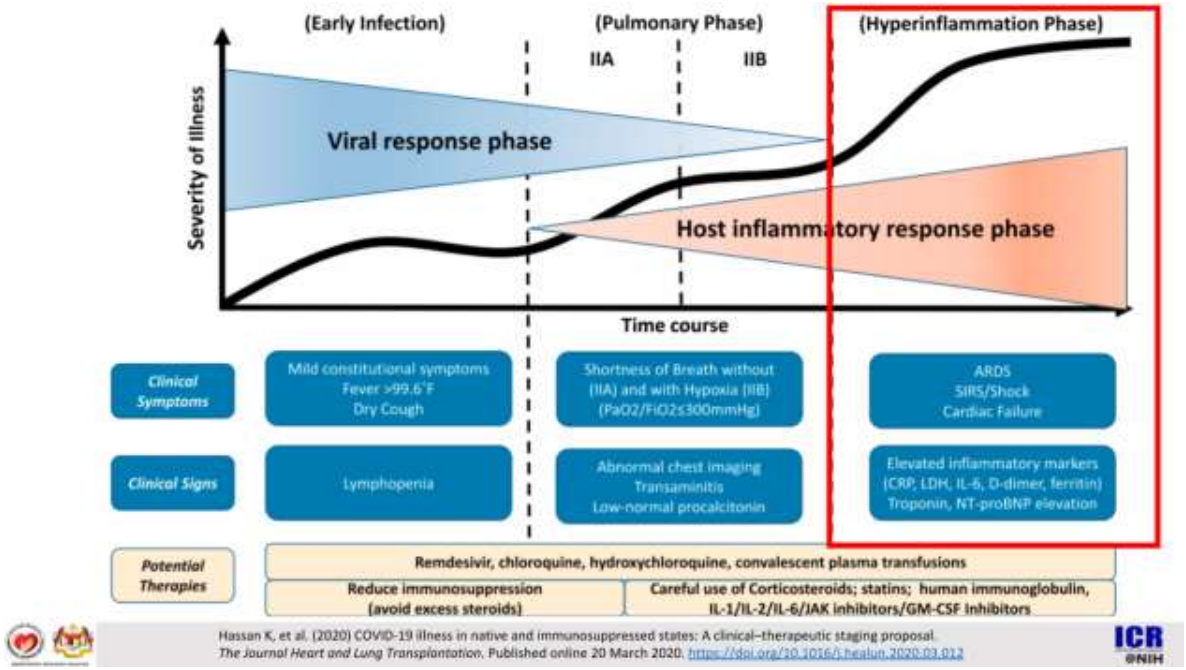

Diagram 6: COVID-19 illness in native and immunosuppressed states: A clinical–therapeutic staging proposal. Link to the slide presentation https://cutt.ly/NyCBn0B

I am going to bring you to this classification of a COVID-19 that was proposed by Hassan et al[5]. There are three phases. We're going to focus on the hyper inflammation phase. This is the end phase in which the host inflammatory response at the greater end and the virus effect/viral response phase are ending. In the hyper inflammation phase, the patient developed acute respiratory distress syndrome, shock, cardiac failure and all the important information markers will be elevated such as CRP, LDH, interleukin 6, D-dimer, ferritin and cardiac markers such as troponin T and NT-proBNP.

Pathogenesis of lung damage

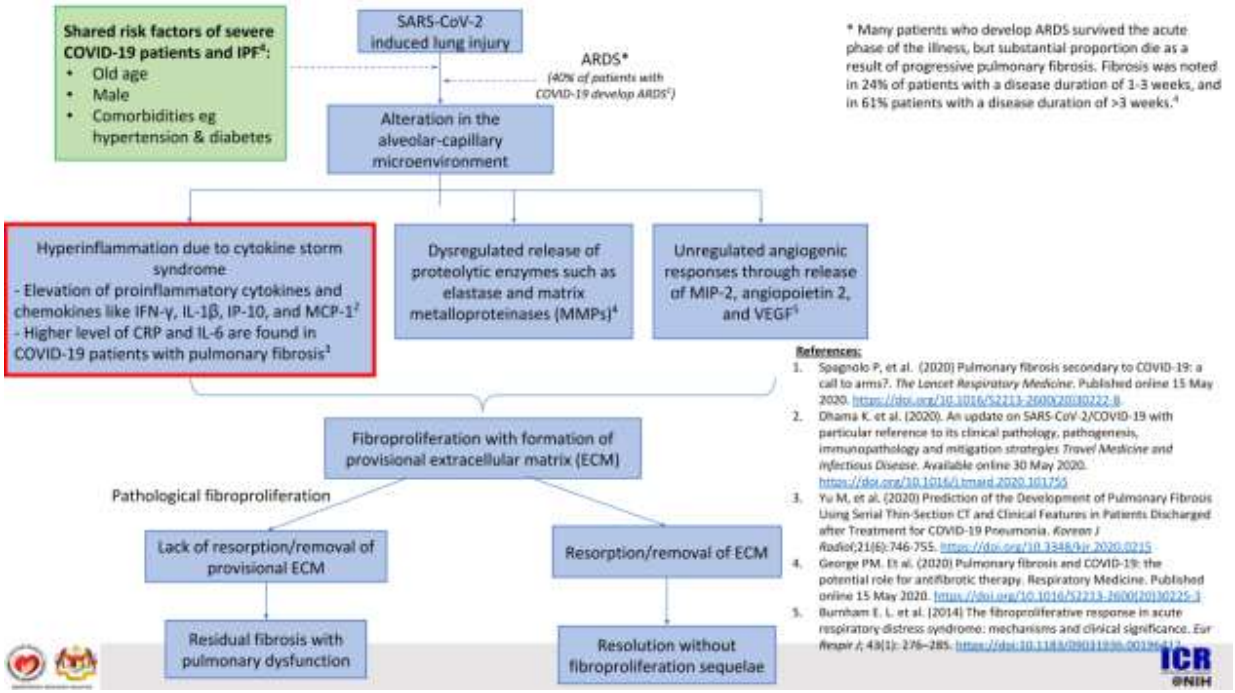

Diagram 7: Pathophysiology of SARS-CoV-2 induced lung injury. Link to the slide presentation https://cutt.ly/NyCBn0B

I would like to bring you to the pathogenesis on how the lung damage occurred in a patient who is infected by SARS-CoV-2 or COVID-19 patient. The SARS-CoV-2 induced lung injury. The SARS-CoV-2 is the virus that binds into the Angiotensin Converting Enzyme 2 (ACE-2) receptor, which is mediated by the S-glycoprotein. As it enters, it will go and concentrate at the respiratory tract because the ACE-2 receptors are highly expressed at the lower respiratory tract. There are a lot of alterations in the alveolar-capillary micro environment. So all these processes as mentioned earlier happened in the hyperinflammation phase. This is due to the cytokine storm syndrome where all the pro-inflammatory cytokines are being elevated. And it also caused a dysregulated release of proteolytic enzymes and also unregulated the angiogenic responses. All these three will cause fibroproliferation with the formation of a provisional extracellular matrix. And this process is also seen in patients with idiopathic pulmonary fibrosis. So it's a disease that forms a pulmonary fibrosis which is progressive. You could see this pathway actually lead to a pathological fibroproliferation as what we are seeing in our idiopathic fibrosis patients. So the reason why they progress is that they lack resorption or removal of provisional extracellular matrix. Therefore, there will be a residual fibrosis with pulmonary dysfunction.

In these patients or this cohort, you could actually anticipate because they share quite similar profiles which are: older age, male and with comorbidities especially hypertension and diabetes; they are smoking or former smokers. However, patients

who are out of this demographic: they are non-smokers perhaps they are much younger females and do not have any comorbidities. So they are able to remove all these extracellular matrix pretty well and the lung will resolve without fibroproliferation and you could actually translate it to when we do follow-up. We looked at the radiological resolution on CT scan, there was no evidence of fibrosis and lung function was back to normal.

Wuhan - Radiological findings

A study in Wuhan looking at radiological findings only in COVID-19 patients [6]. They managed to get 81 patients which are divided into four groups:

- Group 1- patients who are actually asymptomatic
- Group 2- patients with the symptom onset less than seven days
- Group 3 – patients who have symptom onset one to two weeks and
- Group 4 – patients who have symptom onset more than two weeks.

So, what they have found on the CT scan based on the group 1, 2,3 and 4?

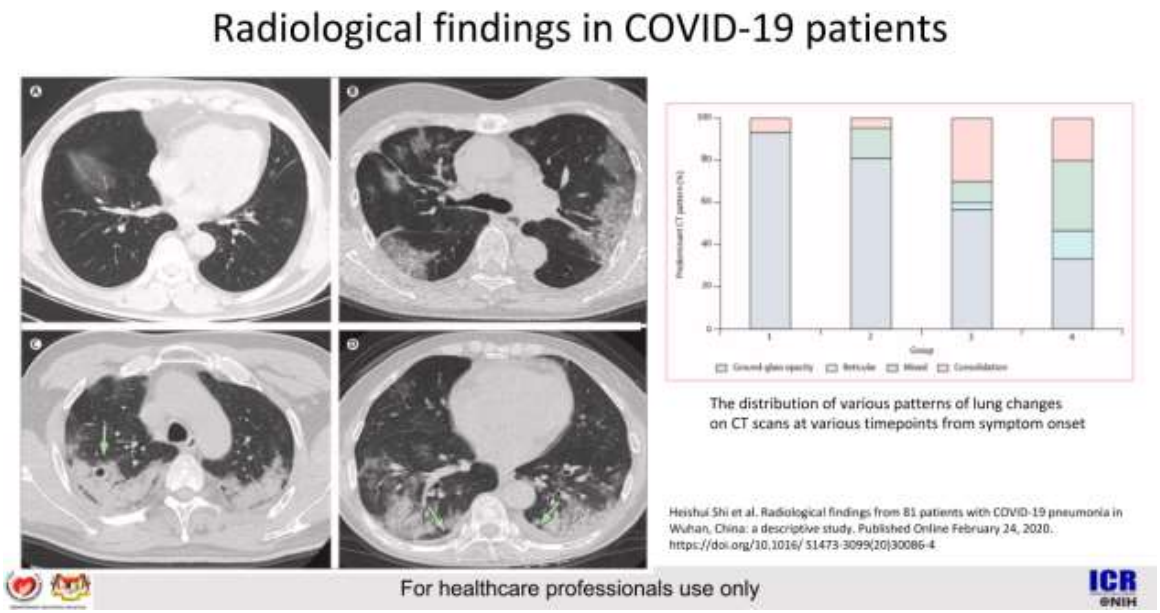

Diagram 8: Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China by Heishui Shi et al.

A. Picture A is a lung CT scan from Group 1. There is focal ground glass opacity associated with very smooth intralobular septa at the beginning and this is at the right lower lobe. It is very focal. So, it is not bilateral infiltrates of the lung because this is an asymptomatic patient. Although asymptomatic, they still have some lung findings on CT scan.

B. If you look at Group 2 which is even more pronounced in CT scan finding as compared to Group 1. There is a bilateral peripheral involvement with a wavy pattern which is shown in this CT section.

C. There is a bilateral and peripheral consolidation predominantly seen in Group 3.

D. The last group is those who had symptom onset two weeks and above. You still see bilateral peripheral involvement but with mix patterns. Now you are seeing perhaps a little bit of reticulation, moderate fibrosis and also with the pleura effusion. If you look at the distribution of various patterns, Group 4 actually has all the four patterns, predominantly a mix type and there is little bit of reticulation. Reticulation means fine fibrosis.

Local experience

I would like to share some of our local experience. We do follow up on the COVID-19 survival patients. These are the cases that I've just seen within this couple of weeks.

Case 1

This is a lady, 49 years old. She is a non-smoker. She has bronchial asthma and confirmed COVID-19 positive. Initially she was intubated in another hospital for asthma for a day and was transferred over and managed to be extubated. Since she was COVID-19 positive, she was treated with hydroxychloroquine and Favipiravir. However, she has a slow persistent viral shedding. So, that's the reason why she was still in the hospital for up to three weeks. She was desaturated one day in the 3rd week of illness. She was started on IV hydrocortisone based on a report of her CT scan.

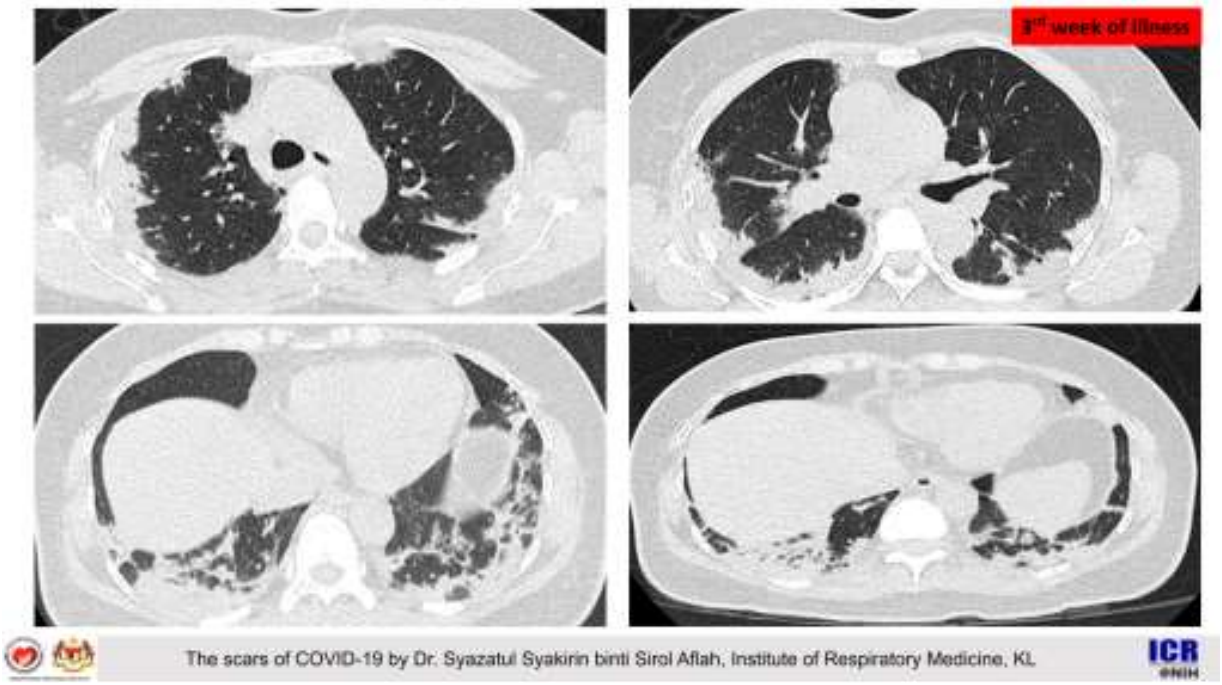

Diagram 9: Lung CT scan finding of case 1 by Dr. Syazatul Syakirin binti Sirol Aflah, Institute of Respiratory Medicine, KL.

This is her CT scan (diagram 9) at the 3rd week of illness where she had virus shading. Even though it was positive, it is not infectious. This is a residual lung damage that occurred in the COVID-19 patient. There was peripheral consolidation and at the bases; you could see a perilobular pattern which is an organizing pneumonia pattern of fibrosis in the CT section.

Seen in the clinic after 6 weeks

We saw her six weeks after she was discharged from the hospital. She was extremely well, no cough and no breathlessness. She started to work as usual. In her recent chest x-ray, we could appreciate peripheral, very subtle consolidation over the peripheries on the left lung. There is a restrictive pattern from the lung function test: FVC: 64% (1.84L), DLco: 59%. FVC and DLco of less than 80% are considered a restrictive ventilatory defect. Even though she had no symptom and her chest x-ray was almost resolving radiologically, she still demonstrated restrictive ventilatory defects on lung function. In her six-minute walk test, she can walk up to 500 metres and the desaturation was not significant as the lowest value was 93%.

Case 2

This is a 70 years old Malay non-smoker woman. She is an elderly woman with co-morbid. She was diagnosed with COVID-19 positive. She was intubated for two weeks, mainly for respiratory failure. She didn't actually undergo any form of dialysis. After one month of hospitalization, she managed to be discharged without any oxygen support.

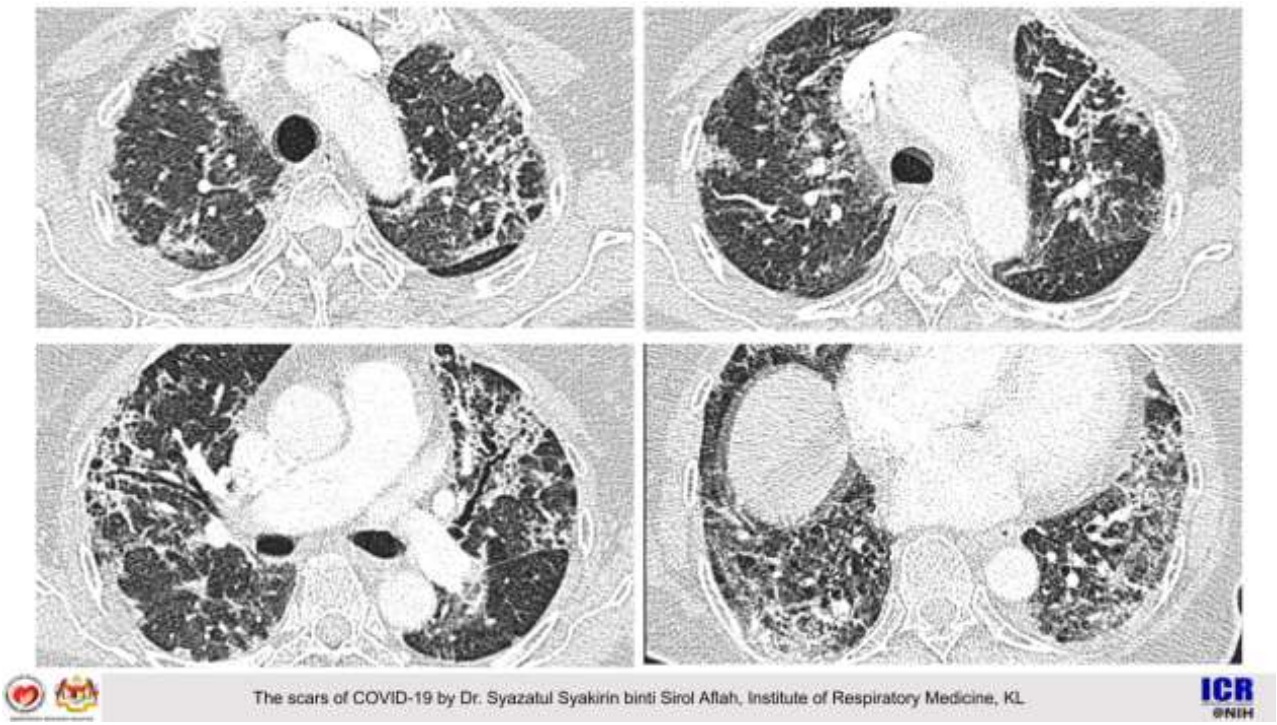

Diagram 10: Lung CT scan finding of case 2 by Dr. Syazatul Syakirin binti Sirol Aflah, Institute of Respiratory Medicine, KL.

Her chest X-ray at the 3rd week of illness, you could see is a lot of lines. All these lines represent fibrosis. When we looked at the CT scan, from thoracic Inlet to thoracic outlet and from apex to the base of the lung, you can see all these white lines which are all the fibrosis. This is what we called a pattern of fibrotic organizing pneumonia. You can see the jagged bronchial wall here which is called traction bronchial disease where the scar of the lung is pulling the bronchus, so it becomes more prominent.

Seen in the clinic after 6 weeks

Her latest chest x-ray compared to the first x-ray taken at the 3rd week of illness, the lines were almost disappearing, and she was asymptomatic; can do house chores as usual, but her lungs have very minimal crepitation at the right extreme base. She also demonstrated restrictive patterns on the lung function, but on the walking test, she did not actually demonstrate any desaturation.

Case 3

This man is a non-smoker with co-morbid and COVID-19 positive. He was warded and on oxygen support, never intubated and was treated with Kaletra and hydroxychloroquine. He was discharged well. However, he was readmitted to hospital because of breathlessness. During the second admission, he did not require any oxygen support. At the second admission, also the 4th week of illness, to be precise, we managed to get a High-resolution CT chest for him. So, what have we found?

Like previous cases, we found all these lines on the HRCT chest, representing fibrosis with peri-lobular patterns which is an organizing pneumonia pattern of fibrosis. The lung volume showed a slight reduction and it was more pronounced on the right as compared on the left. There is a ground glass appearance with fibrotic bands.

Seen in the clinic after 6 weeks

Six weeks after being discharged from the hospital, he was asymptomatic, able to exercise, lungs were clear and lung function is back to normal. This was pretty fast and this could be because he was not intubated. He managed to walk up to close to 600 meters and desaturated at about 93%.

In his latest chest x-ray, we found an area representing fibrosis. We're going to repeat the HRCT chest to look at the detail of it and compare it to the first HRCT to see whether it is resolved or not.

Case 4

The fourth case is a 68 years old man, a former smoker with comorbidities such as Ischaemic Heart Disease on pacemaker and chronic obstructive pulmonary disease. He was in ICU for two months, intubated with tracheostomy. He received a number of treatments: Kaletra, Hydroxychloroquine, SC interferon and IV dexamethasone. At the fourth or fifth week of illness, he was given IV methylprednisolone only one dose because he was then complicated with upper GI bleed and sepsis. He was treated with courses of antibiotics. They managed to wean him off from the ventilator and he was on a tracheostomy mask upon transfer to the ward for rehabilitation. However, after staying a day or two, he was well under room air and now he is actually mobilizing on a wheelchair after two months being in ICU. He had CT thorax at fourth week of illness and a repeated CT thorax recently, six weeks later.

CT Thorax at 4th week & 6th week

CT thorax at 4th week, there were a lot of lines or lines of fibrosis seen, and he had bilateral pleural effusion. The fibrotic changes at the middle region were more prominent on the right compared to the left. At the bases, it looked horrendous: the fibrosis (a lot of white lines) and pleural effusion. The traction bronchiectasis was visible at the bases which showed the degree of the fibrosis and reduction of the lung volume.

There was no pleural effusion and less white lines (fibrosis) seen at 6th week. At the middle region, we can see lung resolution of fibrosis, with only minimal reticulation that can only be appreciated on the CT scan. The bases looked much better and lung volume was better when compared to the scan from fourth week.

Case 5

This is a 73 years old man, former smoker with COVID-19 positive. He was intubated for nine days with severe acute respiratory distress syndrome (ARDS). He received treatment, extubated and was discharged home. However, he was readmitted for breathless on exertion. He was warded for a few days and transferred over to *Institut Perubatan Respiratori* (IPR) for further management. Clinically, there was no finger clubbing. However, as for the lung, there was a pronounced Velcro sound heard bi-basally. No pedal edema or no sign of heart failure.

His lung function demonstrated a restrictive pattern of less than 80%. He did not actually walk that far. That's why we could not demonstrate desaturation. He tried to preserve his energy and only managed to walk up to 120 metres. His arterial blood gas under room air result showed he didn’t require oxygen therapy, but it's the breathlessness that is problematic to him.

Chest X-ray

His chest-x ray on admission in the hospital was a portable chest x-ray which is difficult to comment as the image is not clear. But, the subsequent chest x-ray, there were fine lines. These fine lines are translated to fibrosis. The latest one that we had in X-ray are even more pronounced fine lines. So, you could actually appreciate a reduced left hemi-thorax volume as evidenced by the elevated left diaphragm. The left diaphragm was pulled by the fibrosis/fibrotic scarred lung.

CT scan at 4th and 6th week of illness

The CT scan was done at the fourth week of illness and another one at six weeks later. The first CT scan at 4th week, there was a reticulation at the peripheries (fibrosis). At 6th week, the lines were finer when compared to 4th week. Subsequent sections of CT scan of 4th week showed the ground glass opacity with dense, perhaps dense consolidation. At 6th week, we can see even fine fibrosis with perhaps a small fraction of bronchiectasis and all these are evidence of a significant fibrosis. At the bases, we could even see more pronounced fibrosis here on the latest (6th week) CT scan.

If you look at the pattern of the fibrosis and compared to the other four patients, the three of them had almost complete radiological resolution. Only one patient in between. But, this patient (case 5) has worsened in terms of the fibrosis. We hypothesized that he might have a pre-existing interstitial lung fibrosis to begin with and on further questioning with him, he did experience breathlessness since 2018 with the dry cough. However, he went to a hospital to be investigated for a heart problem, but he was told his heart was okay, but was not told that he had a lung problem.

So, these are the five patients, a small limited experience by the local.

Article: Follow-up studies in COVID-19 recovered patients. Is it mandatory?

I would like to put up this paper/question: “Follow-up studies in COVID-19 recovered patients. Is it mandatory?[7]” Well, to say it is mandatory, it is difficult, but I think it should be proposed and should be done. I would say “yes, of course.” When we look at the patient who has risk to develop progressive fibrosis in the future, especially in a group of patients who are prone to develop fibrotic lungs such as men, former smokers, elderly and also those with comorbidities.

A clinical trial to evaluate the efficacy and safety of Pirfenidone with novel coronavirus infection

So perhaps clinical trials besides studying antiviral, we should explore drug trials such as Pirfenidone, anti-fibrotic properties to slow down or to prevent the process of fibrosis during COVID-19[8].

Summary

As a conclusion, post-viral fibrosis caused a substantial physiological impairment that was documented in previous coronavirus outbreaks. Thus, a close follow-up of patients after COVID-19 is essential. A global burden of fibrotic lung disease will probably increase considerably as fibrotic lung disease following the SARS-CoV-2 infection burden is likely to be high. To alleviate severe COVID-19 complication, it is a call for an urgent need for therapies and clinical trials of anti-fibrotic molecules should be considered.

Slide link: https://cutt.ly/NyCBn0B

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“COVID-19 and Kawasaki Disease” by Dr. Hung Liang Choo, Hospital Tunku Azizah, Kuala Lumpur

General Information

Thank you, Dr. Goh, for the kind introduction. I would also like to thank NIH and CRC for inviting me to share information on Kawasaki Disease and multisystem inflammatory syndrome in children (MIS-C) which can probably be associated with COVID-19.

So, I would give a brief overview of what is Kawasaki disease, and to share some literature on MIS-C. As mentioned earlier by Dr. Goh, we do not see any Kawasaki Disease-like Illness in our COVID-19 children. We will go through the possible aetiology of Kawasaki Disease, pathophysiology, how do we diagnose Kawasaki Disease and the treatments during acute phase. Then, I would review the literature from MIS-C and how should we go from here.

Kawasaki Disease

Introduction to Kawasaki Disease

As we all know, Kawasaki Disease is actually an acute, self-limiting systemic vasculitis. It occurs predominantly in infants and young children. If you look at this bar chart (Diagram 11), this is the statistics from Malaysia's Kawasaki Disease Registry from 2010 to 2016.

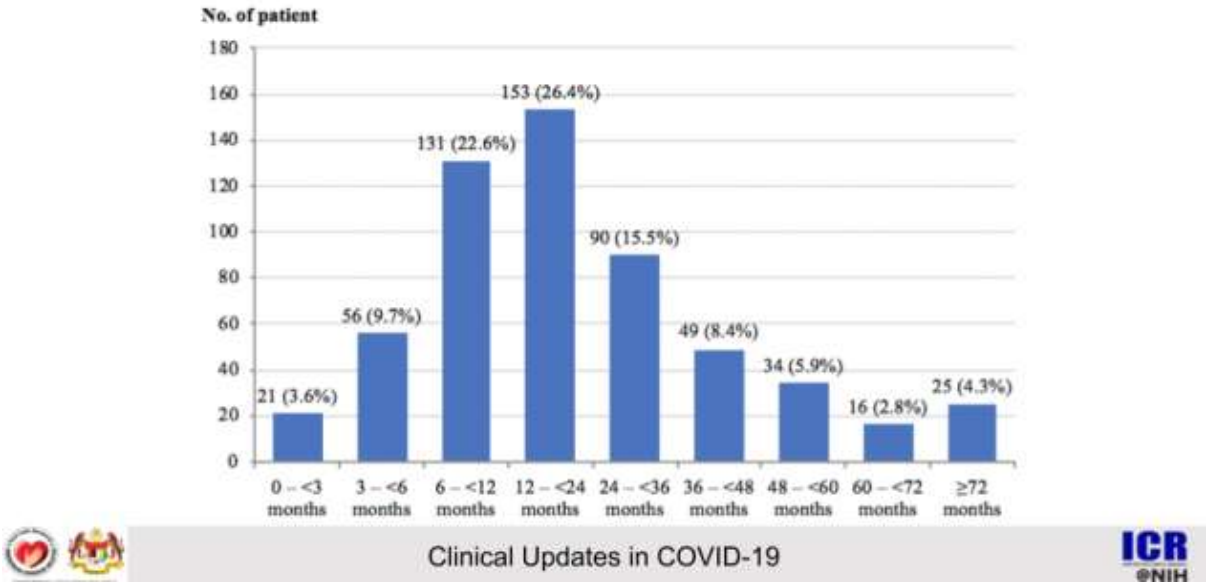


Diagram 11: Distribution of age at onset of illness for patients with Kawasaki Disease in Malaysia from June 2010 to December 2016

You can see that this registry registered all children from 0 to 12 years old. Less than 5% of the patients were above 5 years old. A third of the patients were infants less than 12 months old, and about a quarter were 1 to 2 years old. If you put children below 2 years old, it constitutes more than half of 60% of Kawasaki Disease in this country.

Kawasaki Disease is the commonest acquired heart disease in children in developed countries, and it is the second most common systemic vasculitis in children after Henoch-Schonlein purpura.

History of Kawasaki Disease

Kawasaki Disease is quite a young disease. It was described by Dr. Tomisaku Kawasaki in 1967 in the Japanese literature, and it was translated into English Language Literature in 1974.

Aetiology of Kawasaki Disease

Up till now, despite aggressive investigation and research, we still could not find the aetiology for Kawasaki Disease. What we know now is, it is possibly likely being triggered by some ubiquitous infectious agent(s), and this triggering agent causes asymptomatic infection, triggering immunologic cascade of Kawasaki Disease, and these genetically susceptible individuals will present as Kawasaki Disease. Many viruses were implicated before, that includes adenovirus, respiratory syncytial virus (RSV). I've even seen dengue patients who subsequently developed Kawasaki Disease because of persistent fever and this has been reported in Thailand as well.

The RNA viruses have also been implicated and have been proposed in 2 papers. These 2 papers have suspected RNA viruses could be the cause of Kawasaki Disease, originally. But now we know that it is only a triggering factor and other triggering factors can also cause Kawasaki Disease.

Incidence of Kawasaki Disease

So, in Malaysia, in our Kawasaki Disease Registry, we had a total of 580 patients, and our incidence as a nation was 4.23 cases per 100 000 children under 5 years old in 2011. If we include regional incidence, the highest incidence was around Kuala Lumpur area, and the incidence rate was around 31.10 cases per 100 000 children under 5 years old in 2013. This is comparable to Thailand and the United Kingdom.

When you look at Japan, they do a 2-yearly nationwide survey, and in 2015 and 2016, their incidences were about 300 over cases of Kawasaki Disease per 100 000 children under 5 years old. Kawasaki Disease is very common in Japan, South Korea and Taiwan.

Pathophysiology of Kawasaki Disease

So far, the pathophysiology of Kawasaki Disease is also unknown. There are no pathognomonic clinical features for Kawasaki Disease. As such, there is no specific diagnostic test.

Diagnostic Clinical Features of Kawasaki Disease

So our diagnosis of Kawasaki Disease, still based on what has been described by Dr.Tomisaku Kawasaki in 1967, which is clinical-based. There are 5 features that must be present: (1) clinical feature is high fever, more than 38°C for more than 5 days.

4 out of other 5 features are (2)bulbar conjunctivitis, (3)erythematous rash, (4)redness or cracked lips or oral mucosa, (5)swelling of the cervical lymph nodes, (6)erythema and oedema of the hands, and (7)desquamation of the fingers and toes. Number (6) and (7) are considered as one clinical feature.

These clinical features do not appear simultaneously. In fact, they appear sequentially. So, if you examine the patient at any one time, not all clinical features could be present. We always have to ask from history or questions like “did you notice your child has conjunctivitis?”; if the child has no more conjunctivitis when you examine the child. Sometimes, incomplete Kawasaki Disease is actually classical Kawasaki Disease, whereby the clinical features have resolved.

Classical Diagnostic Clinical Criteria According to American Heart Association

Hence, based on the clinical criteria, American Heart Association (AHA) has recommended that, to diagnose Kawasaki Disease: fever, persisting for 5 or more days AND 4 out of the 5 principal clinical features that we have gone through just now. These children must not have any other reasons to explain the fever. So this is a diagnosis by exclusion. This is because measles can present similarly.

Classification of Kawasaki Disease

If the patient satisfied all the criteria (fever, persisting for 5 or more days AND 4 out of the 5 principal clinical features present), then we classify the patient as having **Classic Kawasaki Disease**. In the absence of all clinical features, this patient would be classified as **incomplete Kawasaki Disease**. If the patient has abnormal or unusual clinical features, and we think that he or she has Kawasaki Disease (no other causes of fever could be found), then we will classify this patient as **atypical Kawasaki Disease**. Usually in this group of patients, the coronary arteries are usually involved to help in the diagnosis. We have diagnosed some of the atypical cases as **Kawasaki Disease Shock Syndrome (KDSS).**

Associated Symptoms of Kawasaki Disease During Acute Phase

Kawasaki Disease also has other associated clinical features. This is due to the pan vasculitis that occurs in these children. Gastrointestinal (GI) symptoms are not uncommon; there could be vomiting, diarrhoea, abdominal pain, gallbladder hydrops. Hepatitis is not common, we did have a child who presented with jaundice, and was finally diagnosed with Kawasaki Disease. They can also present as respiratory symptoms, not common, only about 30% in the literature. Children are usually irritable and this is attributed to aseptic meningitis. Lumbar puncture can show raised lymphocyte count. The patient can have sterile pyuria due to urethritis or meatitis. Arthritis and uveitis can also be present. For infants, we notice that in our series, the BCG inoculation site is erythematous in a high percentage of patients, more common than the cervical lymphadenopathy which is one of the clinical features for diagnosis. In some infants also, there are perianal erythema and desquamation.

Evaluation of Suspected Incomplete Kawasaki Disease

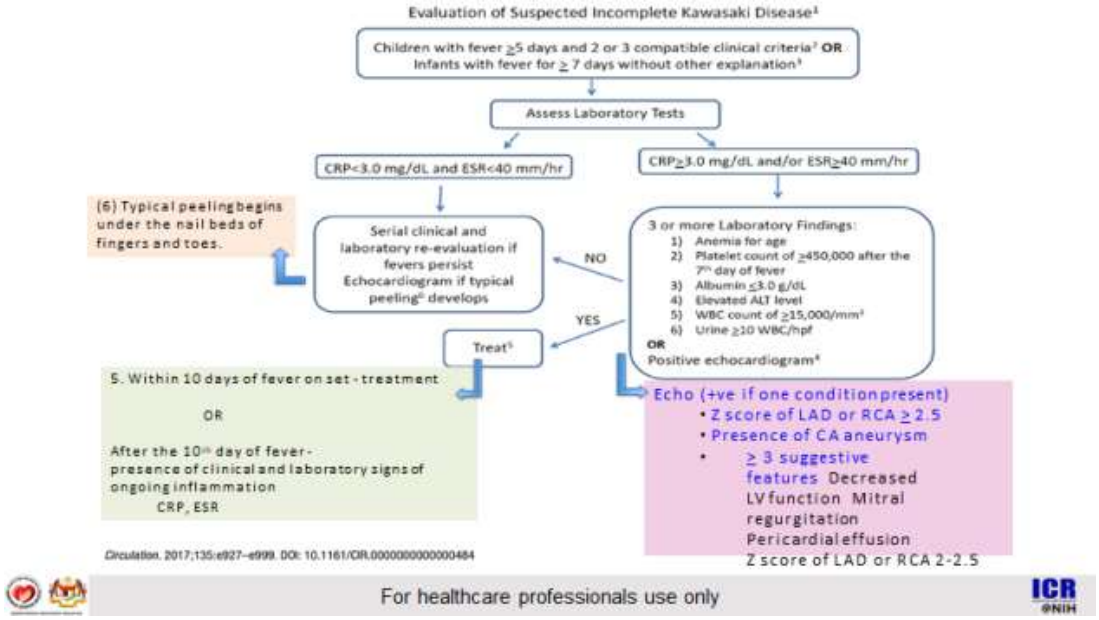


Diagram 12: Evaluation Of Suspected Incomplete Kawasaki Disease

So, if the patient does not have sufficient criteria to be diagnosed as Kawasaki Disease (*i.e.* we cannot find the cause of persistent fever), then we would have to depend on inflammatory markers or blood investigation results to diagnose incomplete Kawasaki Disease. If the patient has a fever for more than five days and two or three clinical features that are compatible with Kawasaki Disease, then we would do inflammatory marker tests like CRP or ESR. If they are raised, we would look for the additional markers like anemia for age, thrombocytosis, hypoalbuminemia, raised ALT levels, raised white blood cell count, or pyuria. If there are 3 out of these 6 conditions, then we will diagnose the patient to have incomplete Kawasaki Disease. In the absence of 3 out of the 6 criteria, we will do an echocardiogram (ECHO) on the patient. If we have sufficient ECHO features to support the diagnosis, then we would diagnose the patient to have Kawasaki Disease, and we would treat this group of patients as incomplete Kawasaki Disease.

If the patient does not have raised CRP or ESR levels, we will have a close watch of the patient and review his or her clinical symptoms again, to see if the patient has Kawasaki Disease. If the patient does not satisfy incomplete criteria, we shall not treat the patient, and keep the patient on close watch. If the patient has typical peeling during convalescence phase, we will conduct an ECHO to make sure that the coronary arteries are normal.

Treatment of Kawasaki Disease (Acute Phase)

The treatment of Kawasaki Disease during acute phase is IV immunoglobulin (IVIG) 2g/kg as a single infusion over 12 hours. Preferably, IVIG should be given within the first 10 days of fever. With this, coronary aneurysm has been reduced to 5% or less. Without treatment, the incidence of coronary artery aneurysm can be as high as 25%.

Concomitantly, we also give an anti-inflammatory dose of aspirin. In most of the Asian countries and in Europe, we give 30 to 50mg/kg/day orally in 3 or 4 divided doses. In some other countries like in the United States, they still give 80 to 100mg/kg/day 6 to 8 hourly. This child will continue the aspirin treatment until the 14th day of illness, or until the patient is afebrile for 48 hours.

IVIG-resistant Kawasaki Disease

Some patients do not respond to IVIG infusion, and this incidence could be as high as 10% to 26%. IVIG-resistant Kawasaki Disease is defined as persistent or recrudescent fever after 36 hours of completion of IVIG.

In this group of patients, we shall give a 2nd dose of IVIG (2g/kg as a single infusion over 10 to 12 hours), or we should add methylprednisolone to the treatment. Some centres use infliximab. There is a study on the usage of Anakinra in this group of patients. In very resistant cases, in some centres, these are the other drugs (Cyclophosphamide, Cyclosporine, Ulinistatin) that have been used. One of the centres uses plamapheresis as the second line drug as well.

Cardiovascular Complications in Kawasaki Disease

What are the cardiovascular complications in Kawasaki Disease? The commonest complications are actually the coronary arteries involvement, about 20%. Other arteries can also be involved, such as axillary arteries, iliac arteries and femoral arteries, but they are not common. We also have a high percentage of patients with myocarditis (clinical or subclinical) about 30% of them. Less than 1% can develop myocardial infarction, especially in patients with aneurysm. So, that is a brief overview of Kawasaki Disease.

Multisystem Inflammatory Syndrome In Children (MIS-C)

Introduction to Multisystem Inflammatory Syndrome in Children (MIS-C)

We do not see any cases of Multisystem Inflammatory Syndrome in Children (MIS-C) in this country. MIS-C was first alerted to the world by the NHS in the United Kingdom on the 24th April 2020. Then the Royal College Paediatrics and Child Health (RCPCH) came out with a guidance on paediatric multisystem inflammatory syndrome temporally associated with COVID-19. The UK group actually published a letter to alert the world that there is a similar Kawasaki Disease-like Illness in COVID-19 patients. I shall share this briefly with you later.

There is also an Italian group that published this paper in Lancet [1]. They shared 10 patients with classic and incomplete Kawasaki Disease. There is another circulation paper from France and Switzerland that shared data on patients who have acute heart failure in MIS-C as well [2].

WHO Case Definition

With all these alerts, WHO finally came out with a standardized definition. This definition is actually evolving. This is what I downloaded from the internet 2 days ago. WHO may just update it every 2 weeks or so.

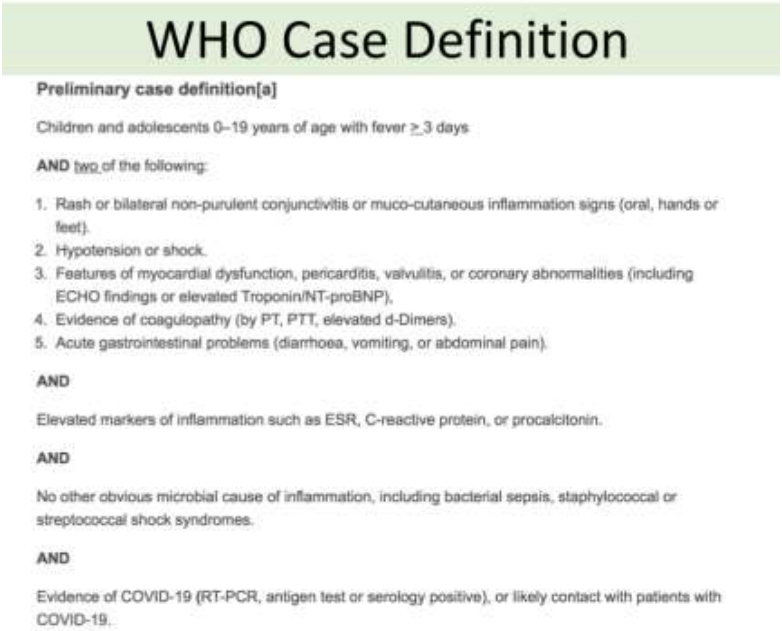


Diagram 13: WHO case definition of MIS-C

The criteria are that children and adolescents 0 to 19 years old of age with fever 3 or more days, AND 2 of the following:

(1) Conjunctivitis and (2)ECHO findings of coronary artery abnormalities are the same as Kawasaki Disease; (3)hypotensive or shock, (4)evidence of coagulopathy which is not seen in Kawasaki Disease, and also (5)acute gastroenteritis problems which is seen more common in MIS-C as compared to Kawasaki Disease.

AND

raised inflammatory markers such as ESR, C-reactive protein (CRP) or procalcitonin, AND

no other obvious causes of inflammation which includes bacterial infection, staphylococcal or streptococcal shock syndrome.

AND

In this group of patients, we must also have evidence that this patient has COVID-19 (*ie.* RT-PCR positive, antigen test or serology positive) or a history of contact with patients with COVID-19.

This is WHO's current definition for MIS-C.

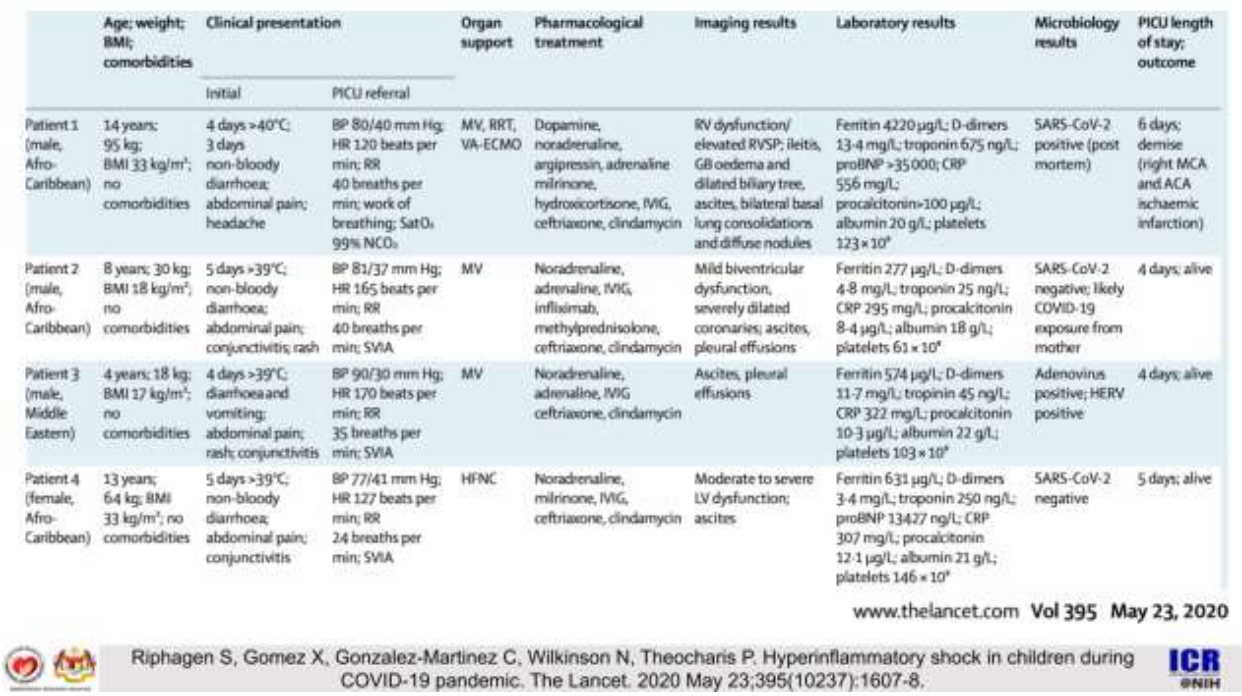
Sharing of Data to WHO Network

WHO has also set up a clinical platform to invite people to share as this is a very rare condition. If you share your data to this network, the data still belongs to the contributor and you may still publish the data that you want. WHO actually encourages everyone to share. There are also many other groups with their own platforms to share as well.

Studies Related To Kawasaki Disease And Multisystem Inflammatory Syndrome In Children (MIS-C)

Hyperinflammatory Shock COVID-19 Pandemic (UK Group)

Coming back to this UK group that first alerted the world about Kawasaki Disease-like Illness in COVID-19 pandemic. They are from London, where they actually serviced approximately 2 million children in the centre of London. They presented 8 children with Kawasaki Disease-like Illness [3]. There are more Afro-Carribean. 6 out of 8 were Afro-Carribean descent, 5 boys (more prominent in boys), 4 had known family history to COVID-19, 2 PCR positive, all were antibody positive. All of them presented with hyperinflammatory shock, either atypical Kawasaki Disease, or Kawasaki Toxic Shock Syndrome. 1 child died of an ischaemic stroke, while another child had a giant coronary aneurysm.



	Age; weight; BMI; comorbidities	Clinical presentation		Organ support	Pharmacological treatment	Imaging results	Laboratory results	Microbiology results	PICU length of stay; outcome
		Initial	PICU referral						
Patient 1 (male, Afro-Caribbean)	14 years; 95 kg; BMI 33 kg/m²; no comorbidities	4 days >40°C; 3 days non-bloody diarrhoea; abdominal pain; headache	BP 80/40 mm Hg; HR 120 beats per min; RR 40 breaths per min; work of breathing; $SatO_2$ 99% NCO_2	MV, RRT, VA-ECMO	Dopamine, noradrenaline, argipressin, adrenaline milrinone, hydroxicortisone, IVIG, ceftriaxone, clindamycin	RV dysfunction/ elevated RVSP; ileitis, GB oedema and dilated biliary tree, ascites, bilateral basal lung consolidations and diffuse nodules	Ferritin 4220 µg/L; D-dimers 13·4 mg/L; troponin 675 ng/L; proBNP >35 000; CRP 556 mg/L; procalcitonin>100 µg/L; albumin 20 g/L; platelets 123 × 10⁹	SARS-CoV-2 positive (post mortem)	6 days; demise (right MCA and ACA ischaemic infarction)
Patient 2 (male, Afro-Caribbean)	8 years; 30 kg; BMI 18 kg/m²; no comorbidities	5 days >39°C; non-bloody diarrhoea; abdominal pain; conjunctivitis; rash	BP 81/37 mm Hg; HR 165 beats per min; RR 40 breaths per min; SVIA	MV	Noradrenaline, adrenaline, IVIG, infliximab, methylprednisolone, ceftriaxone, clindamycin	Mild biventricular dysfunction, severely dilated coronaries; ascites, pleural effusions	Ferritin 277 µg/L; D-dimers 4·8 mg/L; troponin 25 ng/L; CRP 295 mg/L; procalcitonin 8·4 µg/L; albumin 18 g/L; platelets 61 × 10⁹	SARS-CoV-2 negative; likely COVID-19 exposure from mother	4 days; alive
Patient 3 (male, Middle Eastern)	4 years; 18 kg; BMI 17 kg/m²; no comorbidities	4 days >39°C; diarrhoea and vomiting; abdominal pain; rash; conjunctivitis	BP 90/30 mm Hg; HR 170 beats per min; RR 35 breaths per min; SVIA	MV	Noradrenaline, adrenaline, IVIG ceftriaxone, clindamycin	Ascites, pleural effusions	Ferritin 574 µg/L; D-dimers 11·7 mg/L; tropinin 45 ng/L; CRP 322 mg/L; procalcitonin 10·3 µg/L; albumin 22 g/L; platelets 103 × 10⁹	Adenovirus positive; HERV positive	4 days; alive
Patient 4 (female, Afro-Caribbean)	13 years; 64 kg; BMI 33 kg/m²; no comorbidities	5 days >39°C; non-bloody diarrhoea; abdominal pain; conjunctivitis	BP 77/41 mm Hg; HR 127 beats per min; RR 24 breaths per min; SVIA	HFNC	Noradrenaline, milrinone, IVIG, ceftriaxone, clindamycin	Moderate to severe LV dysfunction; ascites	Ferritin 631 µg/L; D-dimers 3·4 mg/L; troponin 250 ng/L; proBNP 13427 ng/L; CRP 307 mg/L; procalcitonin 12·1 µg/L; albumin 21 g/L; platelets 146 × 10⁹	SARS-CoV-2 negative	5 days; alive

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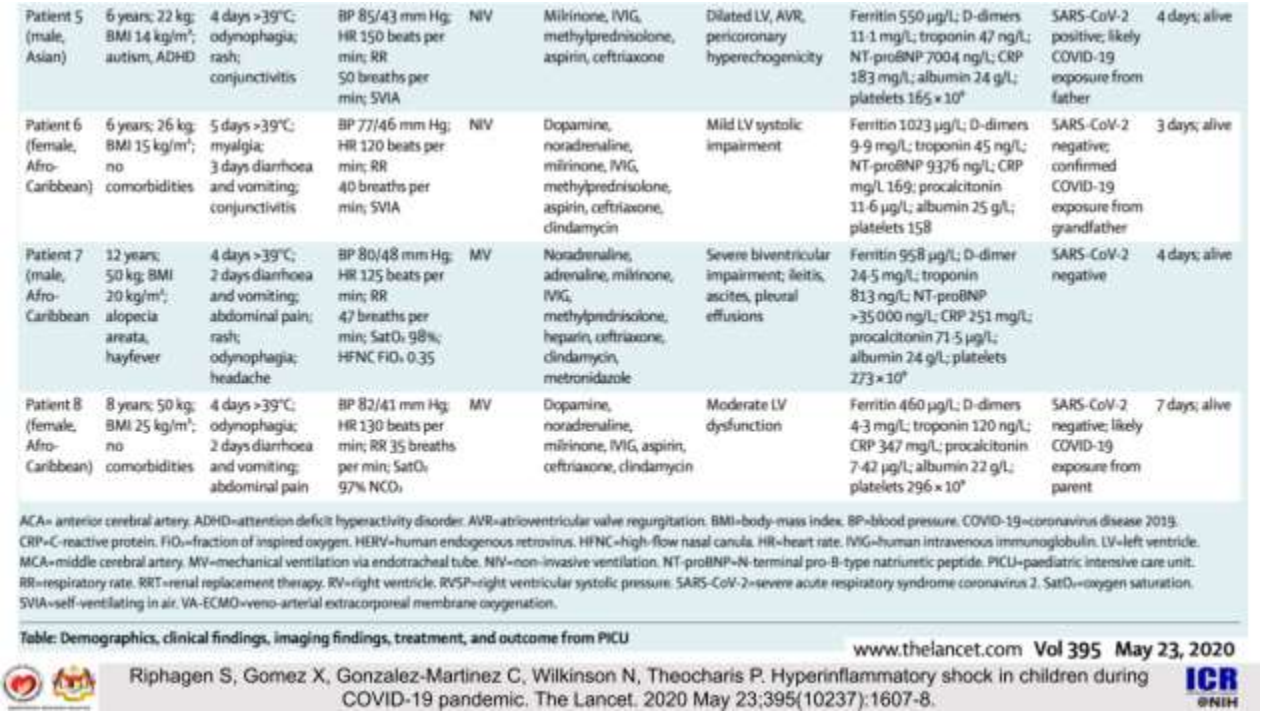
Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. The Lancet. 2020 May 23;395(10237):1607-8.

Table 2a: 8 children with Kawasaki Disease-like Illness from The Lancet - Hyperinflammatory shock in children during COVID-19 pandemic by Riphagen et al.



Patient 5 (male, Asian)	6 years; 22 kg; BMI 14 kg/m²; autism, ADHD	4 days >39°C; odynophagia; rash; conjunctivitis	BP 85/43 mm Hg; HR 150 beats per min; RR 50 breaths per min; SVIA	NIV	Milrinone, IVIG, methylprednisolone, aspirin, ceftriaxone	Dilated LV, AVR, pericoronary hyperechogenicity	Ferritin 550 µg/L; D-dimers 11·1 mg/L; troponin 47 ng/L; NT-proBNP 7004 ng/L; CRP 183 mg/L; albumin 24 g/L; platelets 165 × 10⁹	SARS-CoV-2 positive; likely COVID-19 exposure from father	4 days; alive
Patient 6 (female, Afro-Caribbean)	6 years; 26 kg; BMI 15 kg/m²; no comorbidities	5 days >39°C; myalgia; 3 days diarrhoea and vomiting; conjunctivitis	BP 77/46 mm Hg; HR 120 beats per min; RR 40 breaths per min; SVIA	NIV	Dopamine, noradrenaline, milrinone, IVIG, methylprednisolone, aspirin, ceftriaxone, clindamycin	Mild LV systolic impairment	Ferritin 1023 µg/L; D-dimers 9·9 mg/L; troponin 45 ng/L; NT-proBNP 9376 ng/L; CRP mg/L 169; procalcitonin 11·6 µg/L; albumin 25 g/L; platelets 158	SARS-CoV-2 negative; confirmed COVID-19 exposure from grandfather	3 days; alive
Patient 7 (male, Afro-Caribbean	12 years; 50 kg; BMI 20 kg/m²; alopecia areata, hayfever	4 days >39°C; 2 days diarrhoea and vomiting; abdominal pain; rash; odynophagia; headache	BP 80/48 mm Hg; HR 125 beats per min; RR 47 breaths per min; $SatO_2$ 98%; HFNC FiO_2 0.35	MV	Noradrenaline, adrenaline, milrinone, IVIG, methylprednisolone, heparin, ceftriaxone, clindamycin, metronidazole	Severe biventricular impairment; ileitis, ascites, pleural effusions	Ferritin 958 µg/L; D-dimer 24·5 mg/L; troponin 813 ng/L; NT-proBNP >35 000 ng/L; CRP 251 mg/L; procalcitonin 71·5 µg/L; albumin 24 g/L; platelets 273 × 10⁹	SARS-CoV-2 negative	4 days; alive
Patient 8 (female, Afro-Caribbean)	8 years; 50 kg; BMI 25 kg/m²; no comorbidities	4 days >39°C; odynophagia; 2 days diarrhoea and vomiting; abdominal pain	BP 82/41 mm Hg; HR 130 beats per min; RR 35 breaths per min; $SatO_2$ 97% NCO_2	MV	Dopamine, noradrenaline, milrinone, IVIG, aspirin, ceftriaxone, clindamycin	Moderate LV dysfunction	Ferritin 460 µg/L; D-dimers 4·3 mg/L; troponin 120 ng/L; CRP 347 mg/L; procalcitonin 7·42 µg/L; albumin 22 g/L; platelets 296 × 10⁹	SARS-CoV-2 negative; likely COVID-19 exposure from parent	7 days; alive

ACA= anterior cerebral artery. ADHD=attention deficit hyperactivity disorder. AVR=atrioventricular valve regurgitation. BMI=body-mass index. BP=blood pressure. COVID-19=coronavirus disease 2019. CRP=C-reactive protein. FiO_2=fraction of inspired oxygen. HERV=human endogenous retrovirus. HFNC=high-flow nasal canula. HR=heart rate. IVIG=human intravenous immunoglobulin. LV=left ventricle. MCA=middle cerebral artery. MV=mechanical ventilation via endotracheal tube. NIV=non-invasive ventilation. NT-proBNP=N-terminal pro-B-type natriuretic peptide. PICU=paediatric intensive care unit. RR=respiratory rate. RRT=renal replacement therapy. RV=right ventricle. RVSP=right ventricular systolic pressure. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. $SatO_2$=oxygen saturation. SVIA=self-ventilating in air. VA-ECMO=veno-arterial extracorporeal membrane oxygenation.

Table: Demographics, clinical findings, imaging findings, treatment, and outcome from PICU

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Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. The Lancet. 2020 May 23;395(10237):1607-8.

Table 2b: 8 children with Kawasaki Disease-like Illness from The Lancet - Hyperinflammatory shock in children during COVID-19 pandemic by Riphagen et al.

These are the children presented in the study. The children are from a much older age group, one child is 14 years old while another child is 13 years old. Remember children older than 12 years old in this country (Malaysia) shall be seen by the adult counterpart (physician). Hence the adult (internal medicine physician) should also be alerted of the possibility of Kawasaki Disease-like Illness in this group of children. To highlight the inflammatory marker, they are all raised, I shall not go through much because they are very detailed. I just want to highlight that the age group is older than 5 years old (*i.e.* only 1 child is 4 years old) All of them went into shock, and they needed support, either ventilatory support or inotropic support for hypotension.

An Outbreak of Severe Kawasaki Disease-like Disease at the Italian Epicentre of the SARS-CoV-2 Epidemic: An Observational Cohort Study (Italian Group)

This is the Italian group, an observational study of 10 patients [1]. There are 5 patients with classic Kawasaki Disease whereby they fulfilled all clinical features of Kawasaki Disease, and 4 patients with incomplete Kawasaki Disease. When you look at the age group of the patients, it is also noticeable that patients were in the older age group. There was only 1 child in the group who was 3 years old, and the rest were more than 5 years old. There were 2 patients with enlarged coronary arteries of more than 4 mm, the rest had normal coronary arteries. The ejection fraction for many of the children had low ejection fraction. None of the children were less than 12 months old, hence, infants were not present in this age group. Thrombocytosis is a feature of Kawasaki Disease after the second week of illness but in this group of children, during acute phase, most children actually had thrombocytopenia, which is different from Kawasaki Disease.

This Italian group also compared Kawasaki Disease that they diagnosed before COVID-19, till February 2020 as Group 1 and patients with Kawasaki Disease-like Illness associated with COVID-19 as Group 2. Comparisons were made, and it was found that incidence during COVID-19 of Kawasaki Disease or Kawasaki Disease-like Illness was 30 times more than during ordinary times (Group 1). In this group of patients (Group 2), patients have neutrophilia, and they have lymphopenia as compared to Kawasaki Disease. Platelet count for this group of patients (Group 2) was low, as compared to the classic Kawasaki Disease (Group 1). Inflammatory markers for Group 2 were markedly raised compared to the classic Kawasaki Disease (Group 1). The treatment for both groups are the same, they used IVIG and steroids as well.

The conclusion for this paper is that there was a 30-fold increase in incidence in Kawasaki Disease-like Disease associated with COVID-19, older children, a higher rate in cardiac involvement, immune response to the virus and macrophage activation syndrome (MAS).

Paediatric Acute Heart Failure and SARS-CoV-2 Infection (France and Switzerland Group)

The other group that has written a paper, which is already available online (ahead of print) is the group from France and Switzerland [2]. From 22nd March 2020 to 30th April 2020, they conducted a retrospective study by reviewing a group of 35 children who were presented with fever, acute heart failure and CRP of more than 100 mg/ml. These children are temporally related to COVID-19 as well.

The median age group for this group of 35 patients were 10 years old. You can see that most of the children were older children, and more than half of the patients involved (19 out of 35) were in the adolescence age group. This group of patients might not be seen by the paediatricians in this country. So, the adult physicians have to be aware of this group of patients.

There is a bit of male preponderance. The co-morbid condition like asthma, when compared to the general population, is about the same. There were 6 (17%) of them who are overweight.

Gastrointestinal symptoms are more common in this group of patients as compared to classic Kawasaki disease. 31% of patients have neurological symptoms and 17% had coronary artery dilatation.

By definition, as they included all patients with acute heart failure and ejection fraction of less than 55%. All of them had ejection fraction of less than 55%. About 28% of them have severe congestive cardiac failure with very low ejection fraction (<30%).

The inflammatory markers were all raised, C-reactive protein levels were high, total white blood cell count were high, neutrophil count were high, and interleukin levels were high.

By definition, if a patient has acute heart failure with low ejection fraction, the patient either has myocarditis, myocardial oedema, or myocardial stunning. We can see that troponin levels were raised, and BNP levels were also raised. It is unfortunate that in our government hospitals, we can't do BNP. We have to send our BNP tests to private labs, and the patient would have to pay RM200 per test.

The treatment in this patient group is the same as well, which is immunoglobulin infusion. Some of the patients received corticosteroids as well. Due to the coagulopathy in the group of patients, heparin was used. There was no death in this group of patients.

Conclusion

MIS-C and Kawasaki Disease Associated with COVID-19

MIS-C associated with COVID-19 is quite rare. There are now groups in the United States sharing their experiences in New York City, a new publication from Washington consists of 50 patients in JAMA, but they do not emphasize Kawasaki Disease-like Illness but general COVID-19 in children.

In patients who presented with toxic shock syndrome, it can be with clinical features like febrile symptoms with inflammation, or a full spectrum of Kawasaki Disease, or it can be MIS-C in heart failure as well.

In Malaysia, from February 2020 to 16th May 2020, we have 317 children with COVID-19 below the age of 12 years old. None of them have MIS-C. Most of the children with COVID-19 are mild or asymptomatic.

In conclusion, most of the children with COVID-19 are mild or asymptomatic. This group of children can have the potential to develop very severe diseases especially in infants and adolescents. Many of them actually have cardiac involvement, either as myocarditis or coronary artery involvement. MIS-C itself shares some similarities with Kawasaki Disease but the predominant clinical signs are largely different from Kawasaki Disease, where children are younger age group with skin rash with desquamation, whereas in MIS-C, a lower percentage have skin rash and conjunctivitis. The treatment for these groups of MIS-C patients is the same as for Kawasaki Disease at the moment, that is to use IVIG and steroids and it has proven to be effective.

The Way Forward

The way forward is that we should be aware that in this group of patients with COVID-19 in children and adolescents, they can be mild or asymptomatic, but they can present as severe illness. Initially, from the experience shared to webinar by American and European groups, the patients can be very well and BP would just be slightly low, but they actually went into shock very quickly soon after. Therefore, they suggested conducting a BNP test, which would pick up these mild myocardial dysfunctions early. Hopefully, with this study on COVID-19 associated with Kawasaki Disease-like Illness, we learn more about the pathophysiology of this diagnosis, the genetic predisposition, and the immunology findings. With these findings, hopefully it will help us in our scientific understanding of pathophysiology of Kawasaki Disease.

Thank you for your attention.

Slide link: https://cutt.ly/CyNZaOI

Reference

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“Continuing Care to Cancer Patients during COVID-19 Pandemic-Experience from Radiotherapy and Oncology Department, Hospital Umum Sarawak” by Dr. Voon Pei Jye, Sarawak General Hospital

Introduction

Thank you very much Dr.Goh. Good afternoon to all. My topic for today would be "Continuing Care to Cancer Patients during COVID-19 Pandemic." I would like to share with all of you our experience from the radiology and oncology department in Hospital Umum Sarawak.

First of all, I would like to share the pictures of Mount Kinabalu and Mount Everest. It is not only to please your eyes. At the same time, I am going to give you the reason why I shared these mountainous pictures with you at the end of my presentation.

How Much Do We Know Regarding Cancer and COVID-19?

How much do we know about COVID-19 together with cancer? The data is actually evolving in various fields of COVID-19. For cancer itself, more and more data have been generated.

First of all, it is the incidence of COVID-19 in cancer patients. There is some data coming out from these few epicentres in the world. One of them is from Wuhan, China. For cancer patients, the infection rate is 0.79%, and most importantly we need to know that in the community, the infection rate is only 0.37% [1]. This showed that the data is 2 times higher than the general incidence in the general community.

Other than that, a study was conducted by another epicentre in Europe (Madrid, Spain). We can see from here that there is an incidence rate of 4.2% [2]. We have to see exactly what Madrid's incidence rate is as a whole, which is 0.63%. The incidence rate of 4.2% which is higher compared to the general population.

Higher Mortality Rates of COVID-19 in Cancer Patients?

The next question we would ask is if the complications rates from COVID-19 and are the death rates higher in cancer patients who are infected with COVID-19? The data I am showing here is from China as well. You can see from these graphs (diagram 14), you can see that those with cancer have higher death rates as well as more complication rates from COVID-19 such as ICU admissions, severe critical illnesses and invasive ventilation [3]. Those with haematologic malignancies as well as lung malignancies, when compared to other types of tumours are actually higher.

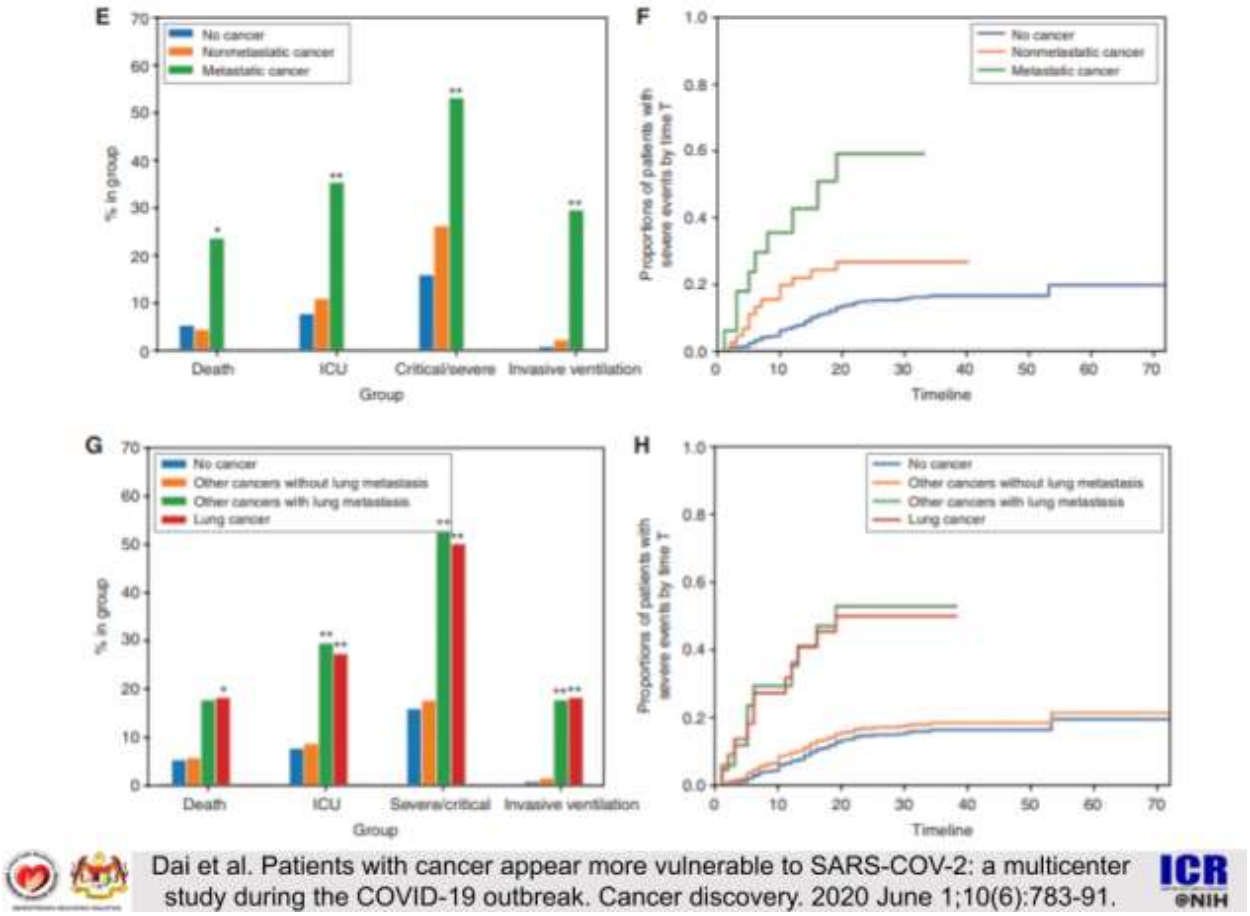

Diagram 14: Charts showing complications of COVID-19 among patients with and without cancer. A study done by Dai et al.

Other than that, another important point is that this paper has highlighted the fact that patients with metastatic diseases actually have higher complication rates from COVID-19 as well as death rates. Those with primary and secondary lung cancer have higher

death rates as well higher complication rates from COVID-19 (*ie.* severe critical illnesses).

When compared to data from the rest of the world, are there similar occurrences seen (*ie.* higher mortality rate of COVID-19 in cancer patients)? The answer is yes. The data obtained from the epicentre in New York City showed mortality rate of cancer patients with COVID-19 was significantly higher when compared to all New York City cases (25% versus 14%). The rate is almost doubled. It is important to highlight that when a cancer patient is infected with COVID-19, there would be higher complication rates and higher mortality rates as well.

The Largest Real World Dataset Investigating Risk of Hospitalization and Death Rates (CCC-19 and TERAVOLT Trials)

a) CCC-19 and TERAVOLT: Population

At this point, we are lucky because we just have the largest real world dataset investigating the risk of hospitalization and death rates of COVID-19 patients with cancer. This was released a few days ago at the American Society of Clinical Oncology (ASCO) annual meeting in the United States. Thoracic Cancers International COVID-19 Collaboration (TERAVOLT) and the international COVID-19 and Cancer Consortium (CCC-19) trials are the largest real world dataset at this point in time.

b) CCC-19 and TERAVOLT: Morbidity and Mortality

CCC-19 trial is a trial which examines patients across all cancer subtypes. However, for the TERAVOLT trial, we only looked at thoracic malignancies, inclusive of lung cancer subtype. What we learnt from these two trials are morbidity and mortality. From the CCC-19 trial, the mortality rate for all cancer subtypes is about 13%, but for those in the TERAVOLT trial, which specifically looked at thoracic malignancy, the mortality rate is about 35.5%. The ICU admissions was 14% in CCC-19 trial and 8.3% in TERAVOLT trial. The percentage of mechanical ventilation was 12% and 5% in CCC-19 trial and TERAVOLT trial respectively.

c) CCC-19 and TERAVOLT: Independent Factors for Mortality

What about the risk factors associated with prognosis? I think it is expected that older patients did poorly as well as those with higher ECOG performance scores (poorer scores). Those with active cancer and currently ongoing chemotherapy also have a high hazard ratio of death and complications from COVID-19.

How Do We Manage COVID-19 Patients During Pandemic Time? What Do the Guidelines Say?

What about guidelines? We have multiple guidelines from international collaboration which have been released in the past 2 to 3 months in terms of how to manage COVID-19 patients with cancer. For example: guidelines from European Society for Medical Oncology's (ESMO) as well as The National Institute for Health and Care Excellence (NICE) guidelines looking into these areas.

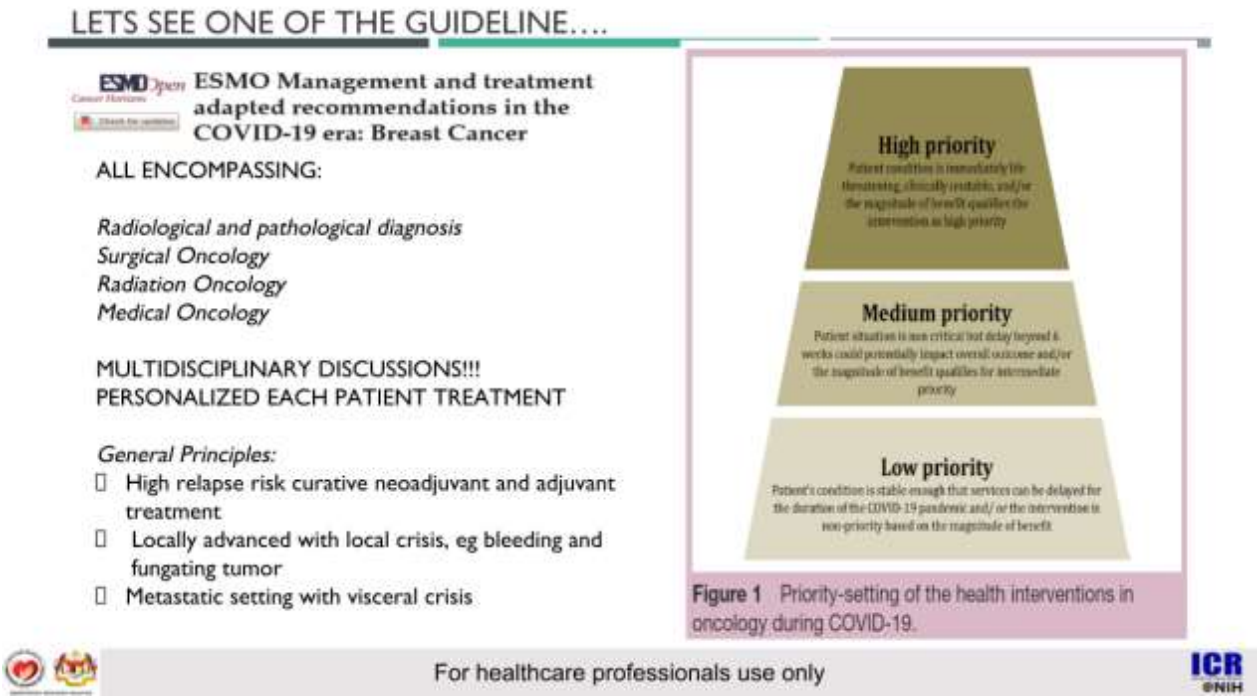

Diagram 15: Guidelines using priority-setting of the health interventions in oncology during COVID-19

I will choose one of the guidelines to highlight its principles and its approaches. For example, the ESMO's Management and Treatment Adapted Recommendations in the COVID-19 Era: Breast Cancer. Most importantly, we should know that this guideline included a multidisciplinary approach; not only oncologist, but also those who are involved in diagnosing cancer: radiology, pathology, surgical oncology, radiation oncology and medical oncology. If you can see from this pyramid, the general principles are to risk stratify all the patients into high priority, medium priority, and low priority, in terms of how we manage the patients and how fast we could manage them. If the

patient is categorized under high priority, the patient should be managed as soon as possible, like the usual emergency type of situations. For patients categorized under low priority, they might even defer treatment for a short period of time for the duration of the COVID-19 pandemic.

Another thing that I wish to highlight is that multidisciplinary discussion is extremely important among all the stakeholders so that we can personalize each patient's treatment plan, risk stratifying them and then treat them accordingly.

The general principle for patients to be categorized as high risk are patients which have high risk of relapse, including those patients who require curative neoadjuvant and adjuvant therapy. The group of patients which also require early treatment is patients with locally advanced cancer (*i.e.* bleeding and fungating tumor). Patients in metastatic settings with visceral crisis also require early treatment.

Radiotherapy and Oncology Centre In Hospital Umum Sarawak

I would like to give a brief introduction on the Radiotherapy and Oncology Centre In Hospital Umum Sarawak, affectionately known as RTU. We are the only comprehensive cancer centre in Sarawak, serving a population of approximately 2,810,000 people. The number of new cases per year in Sarawak is about 2000 cases, across all tumour types. There are about 20,000 clinic visits follow-up per year. Our outpatient centre comprises a clinic / chemo daycare, and a satellite site at Pusat Jantung Sarawak (PJS) as well. Our radiation services include outpatient and inpatient services. In inpatient services, we have 4 wards, which has a total of 109 beds. We have around 200 staff, which include doctors, pharmacists, nurses, medical physicists, radiographers and other allied healthcare workers.

The pictures in diagram 16 were taken before the COVID-19 pandemic. I would like to highlight that the pre-existing situation is definitely not conducive enough to fight the COVID-19 pandemic. The wards are actually very crowded and the space in the wards is small as well. We actually have the enemy of social distancing even before we had to fight the COVID-19 pandemic.

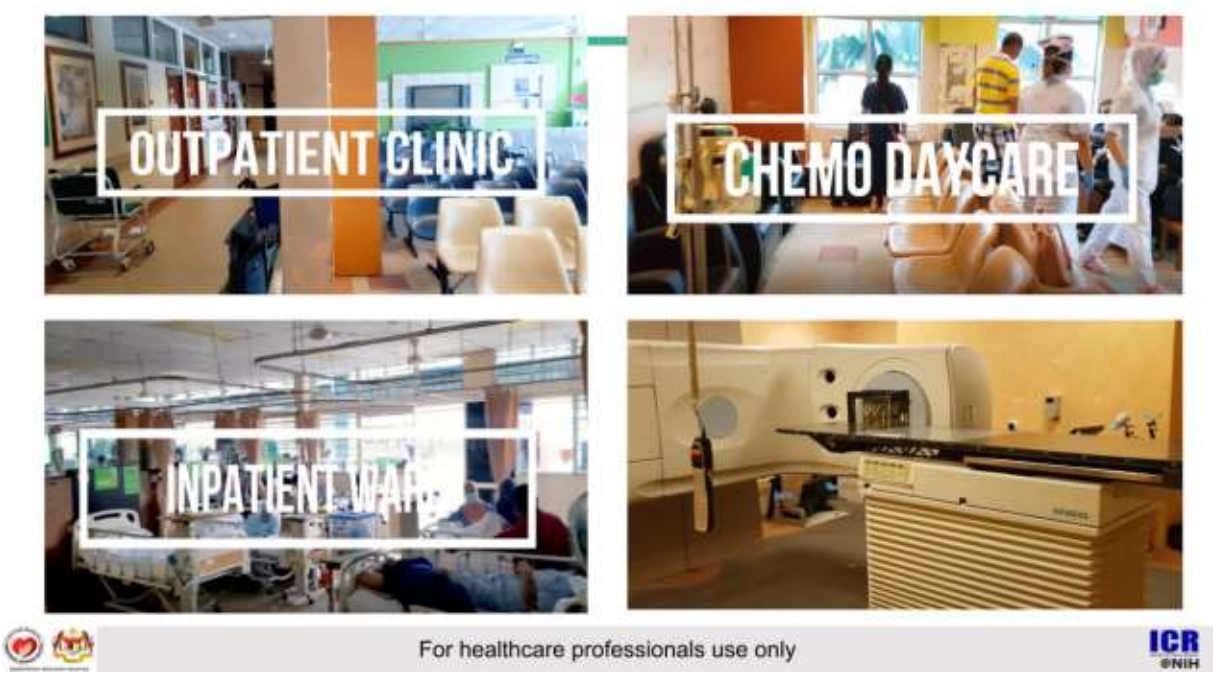

Diagram 16: Pictures from Radiotherapy and Oncology Centre In Hospital Umum Sarawak

Our Experience in Radiotherapy and Oncology Department in Hospital Umum Sarawak

I would quickly go through the experience in the Radiotherapy and Oncology Department in Hospital Umum Sarawak. We are still learning each day, and hopefully we will learn from all of you as well. The most important principle that guides us during this time is actually the fact that we must continue our services. We are the only centre in Sarawak. There is no other place for the cancer patients to go for treatment and care.

The next big question is how to protect our patients and our staff when trying to continue our cancer services during this pandemic? We have identified many challenges. One of the most important challenges is that we do not have any precedence which we could learn from. This pandemic is new for all of us. At this point, after 2 or 3 months, we roughly know more compared to 2 to 3 months ago when the COVID-19 pandemic has just begun. Cancer patients have higher mortality and morbidity. Hence, they are more vulnerable to COVID-19 due to underlying malignancy as well as the treatment we are giving to them. There is also a limitation in space due to the pre-existing facilities and infrastructure, as seen from the previous slide. Indirectly, this led to problems in physical distancing in our department.

Strategy in Handling COVID-19 pandemic in RTU

Our strategy is very simple. It involves teamwork. Let us look into each area.

Identify the problems

We have identified what is the problem in the outpatient department which is overcrowding. We also know that the risk of cross infection is extremely high in outpatient clinics as well as chemotherapy daycare. At the same time, another thing which is probably more peculiar to us is our setup. Many patients came from all over Sarawak to us, and we know that MCO in Sarawak involves inter district lockdown as well. Patients were unable to travel in between districts. We have to try to avoid delays and defaults. So, measures need to be taken.

In inpatient care, we have 4 wards: FRTU, MRTU, ambulatory and palliative care wards. We really have to think on how to prevent cross infection between patients and healthcare workers. The important thing is that we are trying our very best to prevent lockdown and quarantine of staff. From the start, we already have a limitation of bed occupancy and staff. If lockdown happens, we would not have any place to ward our patients.

Other than that, we also have to conduct CME and cancer research during the COVID-19 pandemic.

Outpatient Oncological Care: Overcrowding. A Perennial Problem

In our department, it is very important to ensure that there is an entry point to the department to prevent external attack, which is COVID-19. We have restricted our entry points to 2 entry points in the whole department. Only patients are allowed to enter. If the patients are frail, we allow one carer. We also tightened our screening procedures as well.

Initially, when we first started the screening procedures, we found a lot of gaps when we screened patients. What we did was we identified the weakest links. We used the strongest in the team to take care of the weakest link. We sent out the medical officers for one week to mend this area, so that they could work together with the allied health workers to do the screening procedures. Subsequently, I am happy to say that our allied health workers are very competent in screening patients after learning from each other and with the help of the medical officers as well.

We also practice social distancing in the clinic outpatient area. What we have done is that we reduced the number of patients. We risk stratified the patients (*ie.* looked through outpatient appointments and rescheduled the clinic appointments based on prioritization in accordance to international guidelines). In terms of healthcare workers, we have rescheduled their work timetable, so that they work in teams.

We also decentralized our outpatient care. One of the important things that we have identified earlier on is the overcrowding in our daycare centre. Hence, we have set up another new daycare centre during the initial phase of COVID-19. Before we have two daycare centres and now, we have 3 daycare centres. We set this up within a day, and added 9 chemotherapy chairs. We did it by converting our TV room at one of our ambulatory wards into a daycare centre. We have also deployed more patients to our satellite site at Sarawak Heart Centre for daycare chemotherapy and outpatient day care visits. We prolonged our service time and increased the number of staff at our satellite site. We also redistributed and coordinated our outstation patients from district hospitals to our nearby peripheral hospitals.

Outpatient Oncological Care: Telemedicine

We worked very closely with peripheral hospitals, e.g. Hospital Sibu. We discussed new cases with them through telemedicine. We have trusted liaison medical personnel in handling our telemedicine sessions. We initiated this Telemedicine project last year with the Hospital Sibu, even before the emergence of COVID-19. Hospital Sibu actually sent a medical officer to us to be trained for 4 months. These efforts have been intensified during the COVID-19 pandemic. We are trying to replicate this model to other hospitals in Sarawak. Hopefully, Hospital Bintulu and Hospital Miri would be joining the telemedicine team soon.

Inpatient Care: FRTU, MRTU, Ambulatory Wards, Palliative Care Wards

How do we protect our patients and healthcare workers (HCWs) from risk of exposure to COVID-19, so that we can avoid the lockdown and the quarantine of staff? There should be meticulous planning and effective communication within the team. We need to understand that humans are habitual beings. Therefore, we need to change their habits. We need to increase their communication with them. For example, we should communicate closely with all the matrons as well as other team leaders in the department. If there are staff that are unwell, this needs to be informed early so that we can manage them earlier. Hand hygiene should be practiced at all times. PPE must be worn correctly as well.

There should also be a contingency plan from the start, in which there should be a place for the patients to go to in case of an unforeseen lockdown. Just like in medicine, we learn along the way and there should be a flexibility of changing the plan if it is needed.

Inpatient Care: Internal Implosion

Aside from what has been mentioned earlier, there is a need to avoid any forms of internal implosion. For healthcare workers, there should be a repetitive reminder on the importance of physical distancing amongst healthcare workers.

As for patients, we placed them in a cohort based on the risk of infection. With the help of the hospital support, we managed to build respiratory cubicles in each of our male and female RTUs for patients with respiratory issues. It is quite impressive that we have completed building the area within 2 days. Some of them had a history of travelling, so we would arrange for them to be admitted to the respiratory cubicles. The reason is simple. If the case turned out to be unexpectedly COVID-19, at least we do not need to lockdown the whole ward, instead we just lockdown one of the cubicles. Healthcare workers should be more cautious in managing this group of patients as well.

Other Areas: CME

Our usual CME in congregation has been replaced with a digital platform like Zoom during the COVID-19 pandemic. My colleagues are still presenting weekly Journal Clubs every week via the Zoom platform as well, so that the whole department would be able to follow the events.

During MCO, besides continuing the CME sessions, we came up with a Handbook of Cancer Care titled “ABC of Oncology Care” following the success story of “Sarawak Handbook of Medical Emergencies.” We are currently in our final stages in preparing for the handbook. Hopefully, the book will be released in the next few months. This is part of self-learning for the doctors and the pharmacists when they are writing up the handbook. The input did not only come from our department. The UNIMAS Psychiatric Team also worked with us closely. At the same time, research interns and medical students attached with us also helped in proofreading.

Other Areas: Clinical Trial During Pandemic. How Much Do We Know? The Impacts

In terms of clinical trials, this is a very important area. Many people presumed clinical trials should be stopped during COVID-19. It is inevitable that things have to slow down. However, should they be stopped?

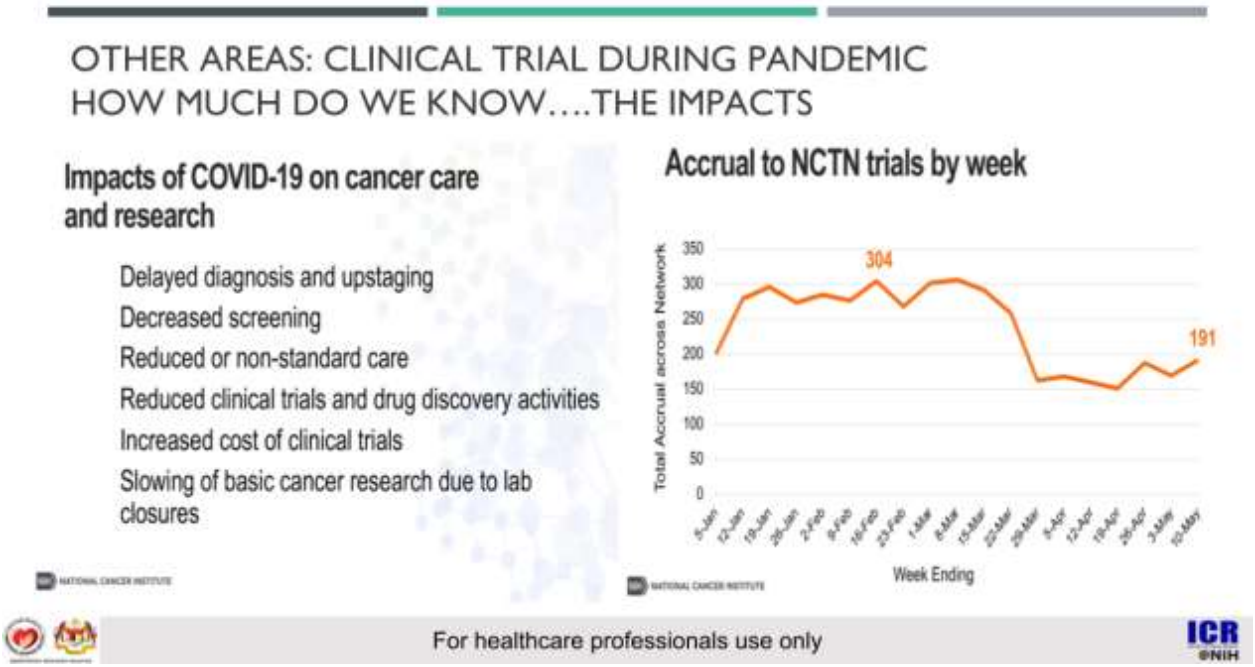

Diagram 17: Clinical trials during COVID-19 pandemic

Let us look into the data in oncological care (Diagram 17). This was also released very recently, a few days ago. The National Clinical Trials Network (NCTN) trials showed that numbers of trials across the network are dwindling but it is not stopping.

Other Areas: Clinical Research In Our Centre

Many trials are still ongoing because these treatments in clinical trials are life sustaining treatment. There is no way that we can stop it. So, how do we deal with it? More effort has to be put in, and we worked closely with the patients, study coordinators, CRA, and sponsors. We did quite a number of virtual visits including a virtual visit with a Sabahan patient who is part of a clinical trial. At the same time, we also shipped some of the oral medications to some of our outstation patients, after obtaining MREC (ethics) approval. We have to address the fear and anxiety of patients and this does not apply to clinical trial patients alone. All these require careful and meticulous coordination.

Challenges. It is Not Smooth Sailing

I have shared with you our experiences and all the measures that have been put in place. However, we still encountered challenges. We were exposed to one of the COVID-19 cases in the open ward that was tested negative initially but subsequently became positive. This incident taught us that we still have plenty of gaps and there is a need to improve our measures. We should always learn to fill up the gaps from day-to-day.

What we have learnt from day-to-day is that we should never forget that our patient is the centre of attention and do not be distracted by the COVID-19 pandemic. We should not forget the primary problem. Instead of cutting down and reducing services, we should intensify our efforts to help our patients.

Cancer Alone VS Cancer with COVID-19

Remember the images of Mount Kinabalu and Mount Everest at the start of the presentation? Metaphorically, we can say, with cancer alone, it already looked like Mount Kinabalu. When cancer combines with COVID-19, it is like Mount Everest. It is already an uphill climb for cancer patients. When cancer patients combine with COVID-19, it is a harder uphill mountain climb. We need to put in more efforts to help them.

One size does not fit all - this is very important as well. What I want to convey is the personalization of treatment. It is important to tailor the treatment according to each individual patient. Even if we have guidelines to help us in managing the patient, at the end of the day, every patient is unique.

Conclusion

Oncologists are generally optimistic people. We should look at the silver lining from this COVID-19 pandemic. It has given us the opportunity to see more clearly the shortfall of our system. In addition, it made us discover that we have "superpower." For example, we can make a new daycare centre within 1 day, and we can build up respiratory cubicles in 2 days' time.

Desperation breeds inspiration. This led us to be more innovative during this difficult time as well. At the same time, we should never forget the research opportunities. The data is generated and presented by all the presenters. This gives us a lot of opportunities, as well as promoting a greater good for patients' care in the future.

Thank you so much.

Slide link: https://cutt.ly/8yCBvQH

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Q&A Session

1. Dr.Narul, recently, there is an article by Lancet (June 2020 Issue) which suggested that N95 masks might be a better option for all healthcare workers rather than a surgical mask?

Dr. Narul: I wish we would be given N95 masks, but the supply to us is not sufficient. Currently, the use of N95 is just for those who are doing sampling for the patient and for doctors who are doing consultations in the fever tent. Due to the limited supply, other healthcare workers are using the 3-ply surgical masks. For those wearing 3-ply surgical masks, they would wear a face shield on it as well.

Dr. Goh: I would like to add that based on an article written by an anaesthetist in Hospital Sungai Buloh who shared his experience in wearing the N95 mask during the early days. A prolonged wear of N95 masks have caused nasal skin abrasion and local inflammation. Hence, there is a need to ensure the N95 masks are put on properly. We need to consult our respective Occupational Safety and Health Administration (OSHA) at our workplace so that wearing the N95 mask would not cause any skin problems.

2. Dr.Hung, since MIS-C has low platelets & reported false negative dengue serology in COVID-19 infection, how should we approach initially (eg. fluid management)?

Dr. Hung: Thank you very much for the question. This is through my reading on Kawasaki Disease-like Illness and MIS-C. We know that some of this dengue serology can cross react and give false positive or post negative COVID-19 results. So, in patients with MIS-C and low platelet counts, this group of patients are usually patients with acute heart failure as well. Therefore, most of them have low left ventricular (LV) ejection fraction. It has been reported that if you give fluids initially, it would not help in the management of the patient as the hypotension would be resistant to the fluid management. LV ejection fraction is low. The treatment would then have to give inotropic support. But for their patients, they were given a fluid challenge with fluid, and it was reported that this group of patients did not respond to fluid management.

From experience, we also know that severe Kawasaki Disease Shock Syndrome, the platelet count during acute phase can be low. In the acute phase of Kawasaki Disease, the platelet count is actually normal. Only in the second week of illness, thrombocytosis would happen. In Kawasaki Disease Shock Syndrome, the platelet count could be low. So, is it part of the cytokine storm that led to the platelet count becoming low? I am not sure. I supposed, for all patients who come with shock, the initial management would be a load of fluid, either 10ml to 20ml/kg, depending on how severe the pulmonary oedema is.

I think a quick echo to look at the contractility of the heart is actually important in this group of patients. In the circulation paper, they actually recommended that in this group of patients who are initially hemodynamically fairly stable, do a BNP. If the BNP level is raised, we should suspect there is myocardial involvement in the patient. It is a bit difficult to do BNP in our context, because the result would not come back in time. Therefore, clinical assessment plus a quick scan for ejection fraction with a small fluid challenge initially.

3. Dr.Voon, to what extent did the practice of "new norm" affect the timeliness and quality of service deliveries?

Dr. Voon: I have to reluctantly admit that it has been affected. We have to look at two areas when answering this question. Firstly, the factors from both the healthcare providers and patients. For the healthcare providers, one of the important things is that the oncology field involves many stakeholders; from the diagnosis part, the pathology, surgical oncology etc. To reserve the capacity in handling COVID-19, some services have slowed down. Then making the diagnosis, staging and working out the disease would definitely be delayed during the COVID-19 pandemic period.

For us, what we can do is try to adapt, to compensate for what was lost during the COVID-19 pandemic period. For example, if we cannot perform surgery on the patient during this COVID-19 pandemic period, we would try to give them neoadjuvant therapy to patients with breast cancer and some of the patients with head and neck cancer. By doing so, patients would still get treatment, and hopefully they would be able to get the definitive surgical treatment subsequently, when the COVID-19 situation gets better.

In terms of the quality of service deliveries, patients' factors play a huge role. There is undeniably a lot of stress and anxiety in patients especially those who have to come to the hospital. The default rate is higher but unfortunately, I do not have any data to support this. This is purely based on my own observation. What we can do is that we are trying our very best to adapt and to prioritize. Hopefully we would be able to reduce the implications. The timeliness of service delivery is definitely affected.

Final Messages by Presenters:

Dr. Narul Aida Salleh

During this COVID-19 pandemic, we as healthcare providers at health clinics should be alert. It would be good if all health clinics can have a designated area for fever centre outside the building so that all these ILI patients can be seen separately from other patients in health clinics.

Dr. Syazatul Syakirin binti Sirol Aflah

From my perspective, I have already talked about the complications of the lung due to COVID-19. Since we have the highest rate of recovery, I sincerely hope that everyone would be vigilant whenever the patient complains about something after they have fully recovered from COVID-19. Thus, a proper referral should be done to us (IPR, KL) or a consultation.

Dr. Hung Liang Choo

I know that COVID-19 in children at the moment in all countries are all mild or asymptomatic. From the sharing of the ASIAN Kawasaki Disease Clinical Research Network, so far, Koreans have seen 2 patients with Kawasaki Disease-like illness, or MIS-C. So far, in other parts of the Asian Pacific region and also in ASEAN region, we do not have any such cases yet. From the webinar, Pakistan did share a case, the rest of the cases are from North America and European regions. I think that this can still happen to our patients in this country, we are now aware of it, the frontliners who are managing COVID-19 patients should be alert and vigilant at all times. If the patient is in compensated shock (*i.e.* blood pressure is still normal but the peripherals are coolish or the pulse pressure is low), we can suspect that this patient may have MIS-C. From the sharing of information at the webinar by the Americans from New York City, they shared that the patients actually would progress very quickly in this state of compensated shock when the blood pressure is normal to uncompensated shock, very quickly, within a short period of time. So, we have to be aware and to watch out for this group of patients.

Another point is that this Kawasaki Disease-like Illness, or MIS-C occurs more in adolescents and in young infants. Therefore, for the adolescents' group, our adult counterpart needs to be more aware as children who are more than 12 years old would be seen by the physicians.

Dr. Voon Pei Jye

I have to reiterate that COVID-19 paired with cancer patients is very real. For cancer patients they are more vulnerable than the general population when they are infected in COVID-19, they also have a higher rate of complications. Due to this, we have to intensify our treatment more in this group of patients. I hope that all of us will not be swayed by COVID-19 and forget about the primary problem (in my aspect) is cancer care for these patients. At the same time, I hope that more and more data would be generated, and with these data, we would be able to manage this group of patients with a better outcome.

Speakers' Brief Bio

Dr. Narul Aida Salleh is a Family Medicine Specialist at Klinik Kesihatan Kuala Lumpur (KKKL). She obtained her medical degree from University of Malaya in 1992, followed by Masters in Medicine (Family Medicine) in 2002. She has special interest in HIV management at the Primary Care level and has successfully set up a HIV/ STI clinic in KKKL. Better known as Dr Nurul among her patients, she is heavily involved with HIV outreach work with a few NGOs around KL. Besides seeing HIV/ STI cases, she also sees and treats chronic Hepatitis C patients, NCD patients and oversees the running of TB and Infectious Disease unit in KKKL.

Dr. Syazatul Syakirin binti Sirol Aflah, is a respiratory physician working at the Institute of Respiratory Medicine, Kuala Lumpur. She graduated from the National University of Malaysia in 2003 and obtained her membership of royal college physician (MRCP) United Kingdom in the year 2010. She pursued respiratory sub-speciality training in Malaysia with further training in Interstitial Lung Disease in Forli, Italy with Profesor Venerino Poletti. She is a member of Malaysia Thoracic Society (MTS), Malaysia Association Bronchology Intervention Pulmonology (MABIP), World Association Bronchology Intervention Pulmonology (WABIP), Asia Pacific Society of Respirology (APSR), International Association for the Study of Lung Cancer (IASLC) and World Association Sarcoidosis and other granulomatous disorders. She is actively in research and participates in presenting oral and poster in local and international congress. Her main interests in respiratory medicine are in obstructive airway disease, tuberculosis and special interest in interstitial lung disease.

Dr. Hung Liang Choo is a Senior Consultant Paediatrician and Paediatric Cardiologist in Hospital Tunku Azizah, Kuala Lumpur. She is currently the Head of the Pediatric Cardiology Unit, and the Deputy Head of Department.

She obtained her MBBS from Universiti Malaya Kuala Lumpur, and MRCP (Paeds) in the United Kingdom. She was awarded the British Paediatric Association Fellowship in Paediatric Cardiology and later worked as a trainee registrar in Paediatric Cardiology in the UK. In 2009, she updated her skills in echocardiography in Boston Children Hospital, USA.

She designed, developed and established the current `Hands-on Basic Paediatric Echocardiography Course' in 2007, and was instrumental in the introduction and implementation of pulse oximetry screening of newborn for critical congenital heart disease in Malaysia in 2014. Her other interests are Kawasaki Disease, Rheumatic Heart Disease, and Marfan Syndrome. She initiated and ran the Malaysian Kawasaki Disease Registry from 2009-2018.

Currently, she is a member of the Asian Kawasaki Disease Clinical Research Network, the President of the Malaysian Paediatric Association and the Deputy Secretary General of the Asia-Pacific Pediatric Association.

Dr. Voon Pei Jye is currently Head and Medical Oncologist with the Department of Radiotherapy and Oncology, Hospital Umum Sarawak, Kuching, Sarawak, Malaysia. He read medicine at Universiti Malaysia Sarawak and graduated in 2001. He undertook training in Internal Medicine and obtained his MRCP (UK) and Master of Medicine (Internal Medicine) from National University of Singapore in 2007. Dr Voon was later gazetted as Internal Medicine Specialist. Subsequently, he completed his advanced specialist training in Medical Oncology from National University Hospital Singapore in 2012.

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