25.05.2021

Learning and sharing session between Dr. Shankara Chetty and Medical Expert Committee

Briefing by Shri. Sampath Kumar, Principal Secretary, H&FW

- An introduction was given on the Medical Expert Committee and it was explained how the committee has been instrumental in understanding patterns of the virus. It was stated that the state has been using the Problem Driven Iterative Adaptive approach where finding solutions tailored to the state's context is given utmost importance.
- A brief description of Meghalaya was given whereby it was stated that there are 7,000 villages dispersed across the State and there is a lot of delay in notifying the disease due to geography. It was stated that Shillong is the main town and it also has limited resources with only 100 ICU beds and 800 oxygen supported beds, out of which 700 are already occupied.
- It was stated that the State has come up with early diagnosis and early treatment protocol; and also put emphasis on providing sensitive support and invest in public and primary healthcare services.

Lecture by Dr. Shankara Chetty

- An introduction was given by Dr. Chetty who is a family practitioner with close relationship with his patients.
- It was stated that early on, there was a realization of lack of understanding of the disease; and due the broad science background, Dr. Chetty understood there no virus has caused so many diverse symptoms. The impression was that this was more than viral infection.
- It was stated that the individual response to the virus was creating the diversity of the virus. It was suspected that this was also some sort of allergic reaction considering the variety of illnesses (multi system disorders) that were seen.
- It was stated that viruses are specific in what kind of tissue they like. This drew attention to the response to the virus rather than the virus itself. From the start, it was observed that this was a respiratory virus and any other symptoms were a physiological response to the virus from individual patient.
- It was decided that a tent would be set up outside the house as ventilation and sunlight is important in dealing with respiratory virus. It was stated that research has shown that contact is an unlikely way of spreading the virus.
- It was suggested that patients should not isolate without seeing a doctor first. Early on in the illness, breathlessness was the focal point. It was noticed that patients felt better by the 6^{th} or 7^{th} day, however on the 8^{th} day people came in breathless. Patients were started on steroids on this day; three to four days after treatment, they showed recovery. Looking at records, first five patients showed breathlessness on 8^{th} day. A lot of effort was taken to establish day of onset of illness.

- It was stated that viral illnesses have a tendency to follow a certain pattern. It was stated that the breathlessness on 8th day had no bearing on the severity of the initial 7 days of illness. Some patients who initially felt completely fine developed breathlessness.
- It was observed that the virus has a two stage process- a non-linear progression and disconnect between the first seven day and what transpired in the 8th day. The only thing that fit this pathogenesis and based on clinical judgement was, this is a type 1 allergic response. The only condition that triggers a severe response to an allergen is type 1 hypersensitivity. The range of the hypersensitivity can go from no reaction, mild &transient, moderate & prolonged, severe & anaphylactic.
- A case was cited where he had a patient with saturation of 80, young, diabetic, and overweight. Looking at this patient, he observed that if this is Type 1 hypersensitivity, because of its onset, it would be wise to add an antihistamine; a children's dose of promethazine was given for a day, the next day, it was observed that the patient was perfectly fine. When the antihistamine wore off, she became breathless again and was again given another dose. Multiple patients have benefited with this line of treatment and Dr. Chetty has seen remarkable progress.
- **The allergic reaction triggered in 3 parts: Respiratory system, Gastrointestinal tract, triggering an allergy in Vasculitis. In type 1 hypersensitivity, the initial response is the release of chemical mediators (histamine, leukotrienes, and platelets activating factors) which if left unchecked can create problems. Aspirin and Montelukast was added to line of treatment. Clopidogrel was also used in some patients.**
- It was stated that there have been patients with 60 per cent saturation levels and considering the lack of hospitals, they had to be managed at home. None of these patients have been put on oxygen and it was stated that oxygen saturation is reversible. The only patients referred to local clinic for oxygen support for an hour or so every day for a day or two when they were extremely breathless.
- With paucity of services available and cheap medication; it was stated that drugs prescribed by WHO and first world nations have not been used.
- **It was stated that a problem that has occurred is patients coming in too late as patients discount symptoms. Any hypersensitivity left unchecked and untreated can cause cell damage and bring about the cytokine storm. By day 12 to 13 hypersensitivity had progressed to hyper-inflammation and cytokine storm. Every patient was educated all patients on importance of day 8 and explained the symptoms to look out for. The most common three symptoms are fatigue on day 8, body aches and pain re-emergence / spiking temperature and breathlessness. It was stated that breathlessness in the first wave presented on day 8; whereas with the second wave, the first symptom is usually fatigue. It was stated that day 8 symptoms is the main cause of mortality and morbidity. It is imperative to recognize the onset and suppress it quickly**.
- Due to weekend closure of clinic, patients were left without medical intervention till Monday; **hence a plan was made and a 'rescue script' was designed which had a combination of steroid, antihistamine and a mild bronchodilator for those who are diabetic. It was explained that they should not take medication before their respective 8th day and only if their symptoms recur/**

worsen. It was also added that if they needed to add the script, they needed to report timeously in order to add/adjust any medication. This was done to manage anything that may transpire with hypersensitivity. Rescue script is a dangerous thing to hand out to patients and can only be given by a doctor after consultation.

- It was stated that on 30.05.2021 will be a year since Dr. Chetty has written this article. It was informed that some hospitals have now followed his line of treatment.
- It was stated that Dr. Chetty considers hospital admission as an outpatient failure and not a necessity.
- It was stated that in South Africa, an education programme emphasizing the importance of the 8th day will be started.
- **It was stated that the illness has a bi-phasic nature. If doctors did not recognize the bi-phasic nature, the understanding of the illness/ drug use of the illness would be out of context. It was stated that the first seven days, doctors are treating a viral infection. It is important to be precise on the day of onset and document this. It is important to help patients understand that the day of onset is the day the patient starts to feel unwell. The change of symptoms is highly predictive on the 8th day which will have implications on patient education and treatment perspective which can save lives and decrease hospitalization rates.**
- It was stated that with hospitals getting on board, it'll be easier to manage the difficult cases and research can be done to assess the difficult cases. It was opined that the difficult cases are the true viral pneumonia cases. These subsets of patients have a dry, persistent and irritant cough for the first seven days. It is Dr. Chetty's understanding that the virus migrates from upper respiratory tract to the lower respiratory tract causing persistent cough; virus gets into their lungs on the 6th or 7th day; and the debris of the virus is then still in the lung; the suppression of hypersensitivity and persistence of the allergen is why it takes time to recover.
- It was stated that senior nurses and junior doctors can be administer treatment and there is no need for specialists early on in the illness. It was stated that only 5 out of 100 will need hospitalization if there is no immediate clinical benefit from the treatment.
- It was stated that with Meghalaya, it is important that all players come on board from a public education perspective (doctors, administrators, quarantine centres in-charge / isolation centres etc.) There should be no disconnect with the facilities and there should be unison. This will allow the proper management of the pandemic.
- It was stated that isolation can cause higher mortality rates as it also means that people would not get critical care on time.
- It was stated that a private practitioners' association training was held in Malaysia with over 200 doctors from India, Singapore and Cambodia also participating. The lecture lasted for more than 6 hours.
- It was stated that in Malaysia if any patient who is tested positive is taken to government isolation for 14 days which prevents people from seeking treatment. The doctors using the treatment method now don't use testing as diagnostic tool but educates any suspected cases on the virus and the importance of the 8th day. CPR and interleukin tests to monitor any blood spikes/ inflammation in the body which justifies change of treatment protocol on the 8th day.

- It was stated that if governments/ regions follow the treatment approach; this can turn the pandemic around.
- It was stated that there is a vaccination push by main stream media and it has been hard to disseminate this information on treatment which has been done primarily through religious leaders.
- It was stated that Dr. Peter McCullough, USA contacted Dr. Chetty and are following his 8th day model and have stated success using this method

Q&A SESSION:

- With regards to comorbidities, it was stated that with the bi-phasic nature of the virus, comorbidity did not play a significant part. It was cited that there were patients' 90 years of age, with stent, diabetic etc. and they had reaction on the 8th day and promptly recovered; however, a patient who was 50 years with no comorbidity became one of the more difficult cases to manage. Comorbidity only plays a part in progression of the disease. There is a genetic predisposition. It was observed that there was no correlation between severity of illness and outcome with the comorbidity, as this is a hypersensitivity (example of bee sting). It was realized early on that there might be a genetic predisposition to the virus. What happens on the 8th day has no relation to the comorbidity; there was no risk stratification based on this. Risk stratification was done based on genetics; eg. if a father had covid-19, his son was educated on the virus and the illness.
- The classification of diseases severity needs to be relooked at considering its bi-phasic nature. Classification should be based on what transpires after day 8 (mild, moderate, severe). It was stated that classification of the viral phase is simple to deal with.
- It was stated that the illness was looked at from a hypersensitivity reaction and there is a production of immunoglobulin E in these patients. Older patients have been exposed to a similar allergen previously and had the reaction to the virus. It was observed that younger population that did not have a reaction were naïve and not affected by the first wave. The younger population who were mildly infected in the first wave and predisposed to the reaction and developed immunoglobulin E subsequently went on to have a hypersensitivity reaction in the second wave.
- It was stated that if this is hypersensitivity reaction, by the third wave, the population will have developed tolerance as with the Spanish flu epidemic and covid-19 will dissipate. It was stated that during the second wave, GI symptoms were rampant. It was stated that the change in spike protein with the South African variant helped the virus have a greater affinity to ACE receptors in the gut causing gastrointestinal symptoms. The spike protein is cause for the hypersensitivity and dependent on the allergenicity of the individual variant's spike protein. This has serious implications for vaccination and its policy. It was also stated that the bi-phasic nature of the virus was not considered during the development of the vaccine. The vaccine needs to be reassessed in this light.
- There should be emergency authorization on medicines that can save people's lives and not on vaccines alone.

- In second wave, 80 mg of steroid was minimum effective dose for the South African variant. This should be assessed if there is no positive response, the dose should be increased. **Doctors from a particular country should come together to form a consensus on the minimum and maximum dose of steroids (which would be on the rescue script accordingly).** The aim is to prevent intubation.
- It was stated that there is a need to increase steroid timeously to show clinical improvement of the patient; it was stated that deferring the increase of dosage will allow mediators to progress and allow cytokine activity which will prolong use of steroid and become more detrimental than a high dose initially to quickly curb the reaction.
- With regards to diabetes, it was advised to never use diabetes as a reason to withhold steroid from a patient. A case of an 80 year old patient who presented with severe breathlessness on the 9th day was cited. Her steroid was increased from 80mg once a day to three times a day; patients with pulmonary symptoms are given ivermectin immediately. This is to clear eosinophilia and showed benefit. Data collected suggested ivermectin has value. She felt better a day or two later, however after a few days her sugar spiked from 8 to 25. Her covid-19 medications were stopped and was started on diabetic medication. She again took a turn for the worse and was hypoglycemic; her oral diabetic medication was withdrawn and her CRP and interleukin levels were raised (as seen in three tests spaced 3 days apart). She was put back on steroids, montelukast and antihistamines and she had a recurrence of fatigue. She was educated on how to manage her sugar values and was put on steroids for a prolonged period. This was six months ago and she is now completely fine.
- It was suggested that doctors try phenergen (promethazine) and if it works continue and if it doesn't, discontinue.

Dr. Andreas Dkhar: Question was asked on use of aspirin in covid-19 patients whose platelets count are already low and on GI symptoms

- Aspirin and clopinogrel have more prophylactic benefit; it cannot be known if it they have prevented the clot or not as these patients will not develop clots.
- A patient with high d'dimer means that the risk of clotting is high, start oral anticoagulant medication like xarelto 15mg 2 times a day and monitor d'dimer till it comes back to the baseline and then decrease the dose to once a day 15mg dose for a full month. At the end of the month, withdraw the xarelto but the aspirin remains. Low molecular weight heparin is for people who present with symptoms of thromboembolism.
- It was stated there is interest in investigating natural remedies in particular to research of gingko biloba (plant).
- A plant called Artemisia to treat parasitic and protozoa infection and used for filarial illness. It has been opined that it is suspected that this plant would be similar to benefits of ivermectin (as an eosinophil)
- With regards to GI symptoms it was stated that from a hypersensitivity perspective, H2 blockers antihistamines of the gut (irritable bowel reactions) was looked at; cimetidine (400mg twice a

day) can be used. Ancillary treatment such as probiotics, electrolytes, hydration is very important. It was stated by Dr. Andreas that famotidine is what is available.

- With regards to the third wave, it was stated that risk stratification of age groups should be done cautiously, it was stated that this is unlikely as if children were to be the more vulnerable group in the coming wave, they would have been susceptible in the current wave also just like the other younger population. The opinion is that the state of development of children's immunity (up to the age of 10 to 12) is naïve and does not have anaphylactic reaction easily as their environment is mostly first exposures. There has been one single case of a 9 year old child with severe GI reaction, looking at his CRP and interleukin levels which were elevated; immediately he was started on steroids and antihistamines and recovered. If dealing with an allergic process, even in its mildest form, this can present itself a few months down the line and should be identified (by skin testing, allergy testing). **Allergy testing is how risk stratification should be done.**

Dr. Sandra Albert: It was asked if in dealing with complexities of myths and misconceptions, is the messaging giving a wide range of information on covid-19 or is it simple messaging in oral form.

It is important for the messaging to come from a reliable and trusted source such as relevant doctors and community / faith leaders in particular areas.

Are there any simple measures in documenting the cases?

There was no time to write prescriptions; on seeing patient for the first time; only the upper respiratory infection date was written and pertinent information. A screening form was put at the front gate which will be shared with the members. A covid-19 pack was structured with simple medication and written on the card plus or subtracted other medication. The staff did the dispensing of medication. Every patient was made aware by instilling a healthy amount of fear / caution of the 8th day.

Dr.Meban Aibor Kharkongor:

- It was stated that the insight on pathogenesis of the disease is very enlightening and has explained many questions and brought clarity.
- Cetirizine is mild and not use for anaphylaxis. It was stated that the hospital will try antihistamines.
- There was agreement on the use of steroid and dosage increase accordingly.
- It was opined whether vaccinating people during the incubation period and at a peak will do more harm than good and this is yet to be understood.

Action to be taken:

- It was requested that a forum be set up to share treatment protocols and learning.
- Principal Secretary, Health will share contact information of Dr. Chetty with the members.

- It was requested that Dr. Chetty to give training to doctors in Meghalaya. It was informed that the village training sessions is open to all doctors and Dr. Chetty will send the link to the modules.
- It was requested by Dr. Chetty to get feedback from the doctors on their positive experiences/ learnings.
- Dr. Chetty to share screening forms and other relevant materials.
- Rescue script to be drafted and used by the State.

No:

(Sampath Kumar, IAS)

Principal Secretary to Health & Family Welfare Department

Government of Meghalaya