# Rare Lives - Why It Is Not Easy To Diagnose A Rare Disease

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In the last episode we covered the impact of the country-wide lockdown to contain the COVID-19 pandemic. This period has been a difficult one for rare disease diagnosis and treatment. But, for people with rare illnesses, many of their challenges during the pandemic have been because of unresolved public health issues. The biggest problem is that only some doctors are able to diagnose rare diseases, delaying treatment significantly. The few doctors who are specialists, often live in India's biggest cities.

Hi! I am Avantika Shrivstava, the host of this show- Rare Lives - a podcast about rare individuals especially during the pandemic. This podcast is a part of the 1 in 20,000 series. For this episode, I spoke with Dr Priyanshu Mathur, a pediatrician at the JK Lon hospital in Jaipur. He handles many cases of children with rare diseases, and I wanted to understand from him the challenges in diagnosing and treating rare illnesses.

Dr Mathur told me about a 20-day-old child who was referred to him from Agra in August. The boy has two severe rare illnesses, which Dr Mathur says is the first such case reported in medical literature, and perhaps in the world. The baby's diagnosis and treatment are telling of the gravity of the problem that rare patients face.

While the rest of the episode is in Hindi, an English transcript is available for you to read. You can log on to the Suno India website to download this transcript.

***Dr Mathur:*** *Ye baccha 20 din ki umar pe wahan pe Agra ke hospital mein admit hua to parents ki ek complain thi ki bacche ko saans mein thodi si takleef ho rhi thi aur saath mein us bacche ke pairo ke movements decreased they. Agra mein is bacche ke diagnosis aur treatmen ke liye prayas kiya lekin phir bhi uske baad uski saans ki takleef barhti gyi aur us bacche ko JK Lon Hospital mein refer kr diya gaya. Jab ye baccha hamare hospital aya us din ye 25 din ka hogya tha. jab maine isko attend kia tab maine dekha ki us bacche ke pairo ka movement bohoti kam they aur uski saans ki takleef bohot zyada thi. humne jo iske initially investigations karaye, to uske andar humne dekha ki us bacche ka heart ka size barha tha jiski wajah se uski saans ki takleef barh gyi thi aur sath mein uske pairon ke andar jo reflexes hain or tone hai wo decreased thi kaafi hadd tak kam thi jab humne is bacche ke initial investigations karaye to uske heart ke andar hame glycogen deposition ki sambhavna lagi jo ki echocardiography se*

*detect hui thi. Tab humne is bacche ko Pompe bimaari ka sandeh jata ke, hamari team ne iski Pompe bimaari ki jaanch ke liye, enzyme ka test bheja. Ye jo enzyme ke test ka report aaya to us report mein hame Pompe bimaari ki pushti hogyi thi lekin saath mein hame doubt tha ki sirf Pompe bimaari ki wajah se uski itni zyada kamzori explain nhi ho pa rhi thi.*

Translation: The child was just 20-days-old when he was admitted in a hospital in Agra. He had a breathing issue and decreased movements in his legs. Even after his diagnosis and treatment there, his breathing difficulty was not cured. He was then referred to the JK Lon Hospital. After initial investigation, it was found that he had an enlarged heart due to which he was suffering from breathing issues. He also had decreased tone and reflexes in his legs/limbs. We suspected glycogen deposition in his heart which was detected through echocardiography. Our team carried out the enzyme test for diagnosing Pompe disease, and through its report it was clear that the child was suffering with it. But his excessive weakness could not be explained through this disease alone.

**Host:** *Pompei ek anuvanshik yaani genetic rog hai jismien glycogen namak ek padarth sharir mein zyaada paya jata hai.*

Translation: Pompei is a genetic illness in which a substance called glycogen increases in the body.

***Dr Mathur:*** *ye baccha spinal muscular atrophy namak rog se bhi peerhit hai to ye baccha ek saath 2 genetic bimaari leke paida hua tha jisme se ek Pompe disease thi jo ki glycogen storage disease hai aur iska jo incidence hota hai, wo ye har 40,000 mein se kisi ek bacche ko hoti hai. Aur jo doosri genetic bimaari thi, spinal muscular atrophy thi jo ki har 11000 mein kisi ek bacche ko hoti hai, khaas baat ye rahi ki ye dono hi bimaariyon ke liye FDA approved treatment available hai aur ye dono hi bimaari aajkal, ilaaj se bacchon ki quality of life ko kaafi hadd tak behtar krne mein ham saksham hain.*

Translation: This child is also suffering from Spinal Muscular Atrophy, so he was born with 2 genetic diseases, one of which is Pompe disease. It is a glycogen storage disease and it occurs in 1 in 40,000 children. The second genetic disease is spinal muscular atrophy whose incidence is 1 in every 11,000 children. The key point here is that there is an Food and Drug Administration-approved treatment available for both these diseases, and these treatments have been able to improve their quality of life.

**Host:** *Bachhe ko dekh kar, Dr Mathur aur unki team ko sandeh hua ki ussey spinal muscular atrophy naam ki bimaari bhi ho sakti hai. Yeh sandeh prashikshan karne par sahi paaya gaya. Spinal muscular atrophy ek aur anuvanshik rog hai, aur yeh maas peshiyon ko kamzor aur nasht karta hai. Donon hi bimaariyaan lailaaj hain lekin vishisht upchaar se durlabh vyakti ke sawashtya ko behtar banaya ja sakta hai.*

Translation: Dr Mathur and his team's suspicion that the child may have Spinal Muscular Atrophy (SMA), another genetic illness, was confirmed with investigation. Spinal Muscular Atrophy weakens and destroys the muscles. Both diseases are incurable but special treatment is available to improve the health of the rare individual.

***Dr Mathur:*** *So main ispe aapko ye batana chahunga ki lagbhag 8,000 durlabh bimariyan hain aur in 8,000 durlabh bimari mein se lagbhagh, 80%-90% bimari hain jo ki genetic defects hain. Ye genetic defect hone ke baad bhi zaruri nhi hai ki ye janam par hi hamare saamne prastut hue. In bachchon ke lakshan janam se lekar even jab ye barhey ho jate hain 30,40,50 saal ke ho jate hain, tab bhi ye pehla symptom leke hamare saamne prastut ho jate hain. Zyadatar genetic diseases halanki bachpan mein apne lakshan dikha deti hain to zyadatar ye patients hamare paas 10-12 saal mein present kr jate hain.*

Translation: I would like to tell you that there are nearly 8,000 rare diseases and amongst these 80-90% of them are genetic defects. Despite being a genetic defect, there is no assurance that it might be visible since birth. The first symptom can be visible at any age, since the time of birth or when a person turns 30,40 or 50 years old. Most of the genetic diseases or their symptoms can be seen in childhood and these patients are then usually 10-12 years old when they visit us.

***Dr Mathur:*** *Aesa dekha gaya hai generally jo rare disease ke patients hote hain, durlabh bimaariyon ke patients hote hain ye bohot zyada suffer krte hain, ye multiple consultations lene ke baad bhi doctors inko pehchaan nhi paate hain. Uski wajah ye hai ki jo, zyadatar durlabh bimaariyan hain unke lakshan alag alag samay pe prastut ho sakte hain, aesa nhi hai ki ye genetic defects hain to ye janam par hi aayenge, kuch bacche hamare paas pehli baar 7 saal, 8 saal, 10 saal, 12 saal ki umar pe pehle lakshan leke prastut hote hain.*

*Doosri pareshani ye hai ki jitne bhi medical colleges hain unki teaching ke andar in durlabh bimaariyon ka teaching curriculum mein samlit nhi kiya gaya tha, jiski wajah se zyadatar doctors inke baarein mein bohot zyada nhi jaante hain. Doosra kyunki ye durlabh rog hain aur inke total number of patients bohot kam hain isliye jo practicing doctors hain unhone bhi in bimaariyon ko zyada dekha nhi hota to inki pehchaan kr pana inke liye asaan nhi hota.*

*Ek important baat ye bhi rehti hai ki inke ilaaj uplabhd nhi hone ki wajah se aur parents ko inke lakshano ke baare mein sahi samay pe pata nhi chalne ki wajah se inme se zyadatar multi organ system involvement dekhne ko milta hai. Inke shareer ke sabhi ang involve ho jate hain aur ye bacche hamare paas doosri bimaari, doosre tarah ke lakshan le karke present ho jate hain. Jaise in bachchon ko baar baar pneumonia hota hai, to ye bacche hamare paas pneumonia mein present ho jate hain, aur hamlog inka pneumonia ka ilaaj krke chutti kr dete hain. Lekin kabhi bhi raredisease ke liye evaluate nhi kr pate hain.*
*Ek aur baat main aapko batana chahunga ki kuch saalon pehle tak inke jo diagnosis ki facilities hain wo bhi India mein bohot acchi available nhi thin but pichle 3-4 saal mein genetic testing India ki centres ki kayi centres pe available hone ki wajah se, ab in durlabh rogon ka pata kr pana hamre liye asaan hogaya hai.*

Translation: Generally, it has been seen that patients with rare diseases suffer a lot (in terms of their diagnosis). Despite having multiple consultations, the doctors are not able to diagnose these diseases. The reason behind this is that the symptoms of these rare diseases do not show

at once, it is not that if these are genetic diseases then the symptoms will show at birth but we have seen children present themselves with symptoms at the age of 7,8,10,12.

Another hindrance is that medical colleges have not assimilated the syllabus of rare diseases in their curriculum so the doctors do not know much about these. Since these are rare diseases, the doctors also do not get to witness many patients and thus are unable to identify them.

Another issue is that since the treatment is not easily available and the parents are also not able to identify the problem with the child timely, these diseases present themselves with multiple organ involvement. Almost every organ gets involved and then the children come to us with different problems and diseases and symptoms. For example, they present themselves with pneumonia and we treat only pneumonia and release them and never evaluate them for a rare disease.

Another thing which I want to add is that a few years back there were no diagnostic facilities for such diseases but now since the opening of genetic testing centres in india, the diagnosis has become easier.

**Host:** *Dr Mathur ne bataya ki Spinal Musculat Atrophy aur Pompe rogon ka nidan jaldi hona khud hi mein ek durlabh cheez hai.*

Translation: Dr Mathur explained how rare it is to diagnose Spinal Muscular Atrophy and Pompei diseases early on.

***Dr Mathur:*** *Spinal muscular atrophy ke bacchon ko jab tak koi bhi doctor diagnose kr pata hai wo bacchen already 5-6 mahine ke ho chuke hote hain. Ye parents doctor ke paas pehli baar tab jate hain jab wo ye dekhte hain ki 6 mahine pe bacche ko baithna shuru krna tha aur usne baithna shuru nhi kiya ya phir usko saans ki samasya hoti hai. Doosra, pompe disease ke bacche bhi generally doctor ke paas jab present krte hain to wo already 6-8 weeks ke ho chuke hote hain, aur pehli baar saans ki takleef leke ya heart ke andar problem hone ki wajah se doctor ke paas pohochte hain.*

*Hamare is case mein jo hamari sabse badi uplabdhi rhi wo yeh rhi, ki humne in dono bimaariyon ka pata is bacche ke 25 din ki umr par clinically humne ye sandhe jata diya tha aur in dono ka confirmatory testing report jo genetic testing humne karayi, aur enzyme testing humne karayi, wo dono report hame is bacche ke 40 din ki umr se pehle mil gyi thi aur ham 44 din ki umr mein ham pompe diasese ke liye isko Enzyme Replacement Therapy shuru kr paye, ye hamari sabse badi uplabdhi is patient mein rhi.*

Translation: By the time a doctor diagnoses a child with Spinal Muscular Atrophy, he/she is already 5-6 months old. The parents consult a doctor when they notice that their child is not able to sit even though s/he is 6 months old, or, has breathing difficulties. Secondly, children with Pompe disease are usually 6-8 weeks old when they are presented to the doctor and these children either have breathing, or heart-related issues.

The biggest achievement in this case [the case of the baby boy] has been that we were able to diagnose and confirm both these diseases before the child was barely 40 days old. And we also managed to start the Enzyme Replacement Therapy for treating Pompe disease when he turned 44 days old and this was our biggest achievement.

**Host:** ***Dr Mathur ne donon rogon se judi vibhin jatiltayon ko samjhaya, aur saral tareeke se maas-peshi ke tone aur reflexes ke baare mein bataya.***

**Translation:** Dr Priyashu explained the various complications associated with the diseases, and also simply explained the meaning of muscular tone and reflexes.

***Dr Mathur:*** *Main aapko ye batana chahunga ki jo pompe disease to patients hote hain ye generelly inka development affect hota hai, ye normal samay pe jo bacche baithna seekhte hain wo 6 mahine ke umar hoti, normal baccha ek saal pe chalna seekhta hai, pompe disease ke bacche normal 6 mahine pe baith nhi pate haain, aur ek saal pe chal nhi pate hain, inka aagey ka development bhi affected hota hai aur apni same umar ke jo doosre bacche hote hain unke comparison mein ye log kaafi peeche reh jate hain.*

*Doosra in baccho ke andar heart ka jo capacity hota hai, blood pump krne ki capacity wo bhi prabhavit hone ki wajah se inko baar baar saans ki takleef aur pneumonia hone ki sambhaavna rehti hai, aur kabhi kabhi cardiac failure, heart failure bhi dekha jata hai. Aur inko baar baar hospitals mein admissions ki jarurat padti hai, agar ham inko enzyme replacement therapy nhi de pate hain to ye zyadatar time apna hospitals mein hi guzaarte hain. Isiliye ye important hai. Aapka doosra sawaal ye tha ki tone aur reflexes ka matlab jo hai wo ye hai ki jab ham bacchon ke haat aur pair ke muscles ke movement ko dekhte hain to jo baccha jo normally muscle strenghth rakhta hai wo kuch hadd tak ham passive movement jo krte hain usko resist kr pata hai but agar bacche ki tone decrease ho jati hai to jab ham us bacche ke haath ko move krenge, to ham asaani se uske haath aur paon ko movement kr sakte hai aur wo bilkul bhi resist nhio kr pata hai. Doosra reflexes ka matlab ye hota hai ki ham jab bacche ki muscles ke contraction ko assist krte hai, stimulate krke to wo contractions jo ki normal insaan mein hote hain, wo bacchon mein decrese ho jate hain.*

Translation: I would like to tell you that the development of Pompe patients is generally affected. Unlike normal children who can sit or are able to start walking when they are a year old or less, children with Pompe are unable to do so, and in comparison with other children they are underdeveloped [delayed in achieving growth milestones associated with children].

Secondly, since the blood pumping capacity of the heart is affected, these children are more prone to breathing issues and pneumonia. In some cases, cardiac or heart failure is also seen. The patients require frequent visit and admissions in the hospitals and without the Enzyme Replacement Therapy, most of their time is spent in the hospitals. That is why it is important.
Your second question was about tone and reflexes. In normal children, if we try to passively move the hands or legs of a child, the child is able to resist but in case of a decreased tone in muscles, they are unable to resist. And reflexes basically mean that if we stimulate and assist muscular contractions in these children, they show reduced activity.

**Dr Mathur:** *Inka motor development affect hota hai, yani inka baithna, chalna, ulte se seedhe hona, seedhe se ulta hona, bhaagna, daurhna, chalaang lagana, apni jo daily activity ke kaam hote han wo apne haathon se kr pana, jaise apna khana khudse kha pana, apna khud se toilet mein jake khud se apna toilet krna, kapde khud se pehenna, kapde khudse khol lena, ye sab kaam prabhavit ho jate hain.*

Translation: Their motor development is affected, like sitting, walking, changing sides, running, jumping, daily activities like eating with their own hands or going to the toilet, changing clothes by themselves, all of these are affected.

**Host:** *Nidan yaani diagnosis hone ke baad bhi ilaaj prapt karna bahot mushkil cheez ho jaati hai. Kaise? Maine ek pita se baat jo ki desh ki paramilitary mein tainaat hai. Inki 5 saal ki bitiya school jaati hai aur apna kaam khud kar paati hai, lekin 4 saal ka beta abhi tak theek se uth bhi nahin pata. Unhone mujhe bataya:*

Translation: Even after diagnosis, getting treatment is a very challenging task. How? I spoke with a father who serves in the paramilitary. His 5 year-old daughter attends school and is capable of doing her own work; his 4 year-old son is not even capable of getting up on his own. He told me:

***Father:*** *Bitiya ko meri ma'am zyada dikkat nahi hai, usko 30%-25% dikkat hai baaki wo har cheez apne aap se krti hai, khati bhi hai, bathroom bhi jati hai, naha bhi leti hai, lekin jaise chalte-chalte wo gir jati hai. Jab gir jayegi to phir apne aap uth jaegi, thoda mehnat karegi lekin uth jayegi.*

*Lekin hamara jo beta hai ladka jo hai, ladka hamara baitha rahta hai, agar wo lete rahega phir usko uthana parhega. agar wo lete rahega, dainey-bain hona parhega to phir usko jo hai karwat badalna parhta hai. Matlab ladka jo mera hai wo apne aap se kuch nhi kr sakta hai. Na wo uth sakta hai, na baith sakta hai, na karwat le sakta hai lekin khata hai, jo khilaenge kha lega, hasega, baat karega, mobile chalayega, har cheez karega.*

Translation: My daughter doesn't have a lot of difficulty. She only faces 25%-30% difficulty but otherwise she is able to do all her daily activities on her own like eating, going to the bathroom, etc. She might slip while walking but after a little struggle, she is able to get back up. But my son isn't able to move or get up on his own.we have to help him move. He can only eat when fed, smile, talk, use mobile phone, etc., but cannot move on his own.

**Host:** Spinal Muscular Atrophy dawaayon ki laagat 4 crore rupay hai. Adhikansh maata-pita ko doctor ki madad se apney bachhon ke liye dawa banane waali company yaani pharmaceutical company ke anukampa upyog karyakram yaani compassionate use programme ki madad se aavedan karna padta hai, taaki dawa company unhein muft mein dawa de sake. Yeh dawaayaian aayat kari jaati hain.

Gopiniyata karan varsh, mein pita ki pehchaan nahin bata sakti hoon. Unse baat karne mein pata chal ki beti ka diagnosis Sitambar 2019 mein hua, woh Lucknow ke bade sarkaari aspataal

mein bhi gaye, aur referrals ki ek lambi kadi ke baad inko Jaipur ke JK Lon aspatal mein bheje gaye jahan Dr Mathur bhi the.

Sochne ki baat yeh hai ki halan ki parivaar aur bachhe Uttar Pradesh mein rehte hai, dawaai mili toh mili Jaipur se. Sabhi zaroori dastavez bane. August mein, mahamaari ke dauraan jab dawaai prapt hui toh pita ko jakar lana pada.

Translation: The treatment for Spinal Muscular Atrophy costs Rs 4 crore. With the help of the doctors, most parents have to apply to the pharmaceutical companies to procure the medicines for free through their 'compassionate use programme'.

Due to confidentiality reasons, I cannot reveal the father's identity. He told me that his daughter was diagnosed in September 2019. He went to a government hospital in Lucknow, and after a long list of referrals he was sent to the JK Lon Hospital in Jaipur where Dr Mathur works.

Of note is that the family resides in Uttar Pradesh, but the medicines were procured from Jaipur [Rajasthan]. After relevant documents were submitted, the father himself had to go and get these during the lockdown (in August).

***Father:*** *To us samay bhi complete lockdown tha na koi jo hai garhi na kuch nhi, phir bhi madam Online jo hai Priyanshu Mathur ne bohot help kari, To kayi document jo hain hame wo bana ke diye to us document ke chalte hamara kaam aasan ho gaya, ki hum jo hain online licence banwayen Kayi bohot saari jo cheezein thin Phir jo hai last jo hai dawai jo hai, saari jab hamari documents complete hogye ban gye to maine Mathur sir ko bataya ki sir aese aese hogaya, sara hamar document tayyar hogaya hai to wo bole theek hai beta, sara jo document hai usko yahan bhejna. To maine madam jo hai sare documents jo hai wo maine_ courier wahan bheja. Aur uske madhyam se jo hai hamari dawai aayi jo Mathur sir ke paas gyi to phir Mathur sir ne hame call kiya dawai aa chuki hai aur aap baki jo hai dawai le sakte hain.*

Translation: Due to complete lockdown, there was no car or anything. Dr Priyanshu Mathur helped us (online). Whenever we used to call him, even if it was morning time or night, he would pick up the call and help us. He helped us with several documents because of which our work got easier. We got a licence and several other documents made online, and Mathur sir helped us a lot. And because of this, we were able to receive all the medicines (from him when he got access).

**Host:** Durlabh rogi ki pratirakshak shamta pehle hi kamzor hoti hai isliye COVID-19 mahamaari mein inko doosron ke mukaable sankraman ka zyaada khatra hai. Mata-pita pe aise bachhe poori tareke se aashrit ho sakte hain toh aur is stithi mein parivaaron ko bahot kathin faisle lene hote hai. Woh kis-kis aspataal jaein aur kab? Kya woh bachhon ka ilaaj rok dein? Dr Mathur ki is par abhibhavakon ke liye kuch rae hai.

Translation: Rare diseases patients already have low immunity, and thus can be more susceptible to the COVID-19 virus. Such children might be fully dependent on their parents, and in this situation families have to make difficult decisions. Some of these are: Which hospitals do they go to and when? Do they stop treatment altogether?

Dr Mathur has a few suggestions for parents.

***Dr Mathur:*** *Meri advice ye rahegi ki jo sabse mahatvpoornh pehlu wo sabse mahatvpoornh pehlu hai in durlabh beemari ke diagnosis to sabse pehle to parents ko ye maloom karna chahiye ki kaun sa center hai jo inki beemariyon ki sahi pehchaan kar paa raha hai taki wo inka sahi diagnosis kar payen. Aur doosra ye hai ki alag alag beemri ke rogi patients ke andar COVID-19 ki severity vary kar sakti hai. Agar unko COVID-19 hota to kuch bachchon me beeamari ki seriousnes zyada ho aur kuch bachchon me jo normal population hai waisi ho.*

*COVID-19 chalne ki wajeh se kaafi saari cheezen affect ho gayi hain aur log apne bachchon ko dikhane ke liye specialist doctor ke paas bhi nahi ja paa rahe hain aur unko dawayian milne me bhi pareshani ho rahi kyunki ye dawayiyan zyadatar internationally import hoti hain to wo bhi abhi prabhavit ho gaya hai. Yeh pareshani humne bhi face ki thi jab Risdiplam dawa humne shuru kari thi pehle patient ko ek maheene pehle shuru kari thi us dawa ko importation me humko zaroorat se zyada samay laga. Lekin is scenario ke andar jo best possible hai wo ye hai ki jahan tak ho sakey ki hum log koshish karte rahen aur doctors bhi koshish karte rahen ki in bachchhon ko treatment ke liye dawayiyan samuchit paryaapt matra me milti rahen.*

Translation: My advice would be that the most important aspect is the diagnosis of these rare diseases. So the parents should know the centres for rare disease diagnoses. And secondly, the severity of COVID-19 [if a rare individual catches the virus] might vary amongst rare disease patients. In some children, it might be severe and while in some the conditions might be normal.

A lot has changed due to COVID-19. Parents are not able to take their children to specialists, and there is a shortage of imported medicines too. This problem was faced by us when we started with *Risdiplam,* which took a long time to become available. The best we can do in this scenario is keep trying our best as doctors and as parents to continue with the treatment.

**Host:** *Jaisa Dr Mathur ne bataya, ek rare disease centre JK Lon aspataal mein bhi hai. Inki ek helpline hai jiska number Suno India website par is episode page mein likha hai.*

Translation: As Dr Mathur mentions, there is a rare disease centre at the JK Lon Hospital. Its helpline number is available on the episode page of the Suno India website.

Helpline number - 7597921472

***This podcast is made possible by a grant from the Thakur Family Foundation. Thakur Family Foundation has not exercised any editorial control over the contents of this podcast***