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PEDICRITICON 2025: Top Articles in PICU Research

In this podcast recorded at the Top Articles of 2025 Session at PEDICRITICON 2025, Dr. Traci Wolbrink interviews Drs. Ashish Agarwal and Ramesh Kumar Ramachandran about two randomized controlled trials. These studies comparing 0.9% normal saline with Ringer's lactate in diabetic ketoacidosis and the efficacy of high flow nasal cannula versus nasal prong bubble CPAP in bronchiolitis. The conversation reveals challenges in resource-limited settings, emphasizing the importance of protocol adherence, mentorship, and resource management. Valuable insights into fluid management, respiratory support, and research execution are offered for healthcare professionals keen on advancing clinical practice and research knowledge.

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Traci Wolbrink *00:11*
Hello. I'm Dr. Traci Wolbrink, a pediatric intensivist at Boston Children's Hospital, and I'm here live on stage in Hyderabad, India at the PEDICRITICON 2025, the 27th National Conference of the Indian Academy of Pediatrics Intensive Care Chapter. I'm delighted to be on stage today doing this live podcast with India's top pediatric critical care medicine researchers of 2025. I'm just going to have the authors start by introducing themselves.

Ashish Agarwal *00:43*
Hello, good afternoon. I'm Dr. Ashish Agarwal. I'm a pediatric intensivist currently working at Cloudnine hospitals at Panchkula. I have done my MD pediatrics from PGI Chandigarh then did my senior residency in PGI Chandigarh, and then my DM in pediatric intensive care from PGI Chandigarh. Currently I'm working as a pediatric intensivist in Cloudnine hospitals in Panchkula, Haryana Street.

Traci Wolbrink *01:06*
Wonderful, lovely to meet you. Ashish.

Ramesh Kumar Ramachandran *01:08*
So good afternoon all. I am Dr. Ramesh Kumar Ramachandran. I am currently working as a consultant pediatric intensivist and associate professor in the medical executive hospital in UAE, Dubai. I was passed out from MD and both DM from PGI, the same from and under the great leadership, Dr. Sunil

Singh, sir. And when the study was conducted, I was the part of the faculty in the institution, and currently I moved to the Middle East. Yeah, thank you.

Traci Wolbrink *01:40*
Wonderful, well, thank you so much. I'm very excited to speak with both of these authors today about their randomized controlled trials. So Dr. Ashish is the first author on the study of 0.9% saline versus Ringer's Lactate as initial fluid in children with diabetic ketoacidosis, a double blind randomized control trial. I was hoping you can tell the audience in maybe two or three minutes about your key findings in the study and what you found.

Ashish Agarwal *02:12*
Thank you, ma'am. So as we all know, we use normal saline day in and day out in our clinical practice, both in emergency and ICU, we use normal saline. But the question is, is this normal saline really normal? So this normal saline, which has a sodium of 154 chloride of 154. It is slightly hypernatremic compared to plasma, but highly hyperchlorimic as compared to plasma. The plasma, which has a chloride of around 100 has a chloride of 154. So it is highly hyperchlorimic as compared to plasma. So there has been this recent talk, and there is a mounting evidence on the deleterious effects of this normal saline, both in critically ill children and adults, also in various settings, like in septic shock or because it is being commonly used fluid for resuscitation. A growing body of evidence suggests that it leads to hyperchlorimic metabolic acidosis, and its deleterious effects on the kidneys also, like it causes renal vasoconstriction and leads to AKI and causes also cause acid base imbalance. This hyperchloremic acidosis is even more important in case of diabetic ketoacidosis. In diabetic ketosis, already they are prone to have hyperchloremia, hyperchlorimic acidosis, because of preferential renal excretion of ketones over chloride. There is a osmotic polyurea. And on top of that, if we give these children, if we treated this children with large volumes of normal saline, this chloride rises and leads to delayed resolution of the DK. So taking this into the background, there was a recent interest in using balanced fluids. So balance is the key mantra nowadays. So the balanced fluids people have used Plasma-Lyte and Ringer's lactate, etc. So what we use the hypothesis was the Ringer's lactate, which has a chloride of around 100 and the plasma also has around so it does not lead to hyperchloremia. Also the lactate anion in the Ringer's lactate goes into the liver, gets converted into bicarbonate, and leading to early resolution of the acidosis. As who also recommends Ringer's lactate as a fluid in cases of acute gastroenteritis, and this is the physiology which which is used at lactate and get gets converted into bicarbonate and leads to early resolution of the acidosis. We use this hypothesis, and we tried this. We tried to randomize the children between around nine months to 12 years who presented to us in diabetic ketoacidosis, we randomized them to receive either normal saline or Ringer's lactate as a fluid, initial fluid, both for resuscitation, also deficit correction. Because in resource limited settings or in developing countries, the scenario is different where most children present late because of late diagnosis, late referral, they present more in severe DK than in milder DK's as in developed countries. So in such children, if we use large volumes of normal saline, this can lead to those problems. So when we randomized, so we plan to randomize these children into normal saline group and Ringer's lactate group. What we found that in the Ringer's lactate group, there was early result of diabetic ketoacidosis. It was around the main duration of the time resolution was 13 hours as compared to 17 hours in normal saline group. So and also the secondary outcomes, like the rise in chloride, the hyperchlorimia at four hours and eight hours of randomization was significantly high in normal saline group as compared to Ringer's lactate group. Also, the rise in bicarbonate was more in the Ringer's lactate group at 12 hours of randomization. So having this pathophysiological basis, this led to our primary outcome, where there

was an early DK resolution in case of now Ringer's lactate as compared to normal saline. So these are, these were the findings, and subsequently, now there has been a recent change in guidelines, also the ISPAD previously used to recommend normal saline, both for resuscitation and deficit correction. But the current guidelines of ISPAD recent guidelines also say if the child needs resuscitation or bolus, then it is better to use balanced fluids, and the deficit correction can be any fluid between .45 to .9% saline.

Traci Wolbrink *06:11*
Fantastic. Thank you so much for highlighting the key features of your study and just a couple quick follow up questions. Have you changed your practice? Do you now use balanced solutions?

Ashish Agarwal *06:23*
Yes, ma'am. So we have changed in our unit. Like ours, is a very busy unit. Like we we operate around five to six hundred percent of the occupancy. We have somewhere around 100 to 120 diabetic ketoacidosis per year. Previously, we used to use more of normal saline, but sub over the last past couple of years, we have we have changed our practice. We are using more of balanced fluids, and we are using more of Ringer's lactate. The challenges in resource limited settings, is to get Plasma-Lyte. It is slightly costly. But whereas Ringer's lactate is readily available, like it is, it is a readily available, cheap fluid which which is commonly being used for acute gastroenteritis. So we have started using Ringer's lactate in place of normal saline in those sick children who present in severe DK and those who are at risk of developing this hyperchloremia and AKI So we have changed this practice.

Traci Wolbrink *07:16*
Fantastic and you use it both for the boluses as well as for the ongoing maintenance fluids as well?

Ashish Agarwal *07:21*
Yes, ma'am, yes. So the deficit correction also the bolus we we use Ringer's lactate.

Traci Wolbrink *07:26*
Fantastic. Well, thank you. And now I'm going to turn to our next speaker, and Dr. Ramesh Kumar, who is an author on the high flow nasal cannula versus nasal prong bubble CPAP in children with moderate to severe acute bronchiolitis, another randomized control trial. I was hoping you could tell us a little bit about your study.

Ramesh Kumar Ramachandran *07:46*
We all know that acute bronchiolitis one of the most common respiratory illness presenting in the emergency and PICU and previously, the standard of treatment is supportive only. Then second thing is the humidified oxygen is the treatment of choice, ultimately. So how we are going to deliver the humidified oxygen, is that question. So previously, we used for this indigenously is made some kind of CPAP system in the setting, in the busy emergency and try to avoid intubation. That is our ultimate goal, because of limited number of liquid weights, particularly limited number of ventilator beds availability. Then most importantly is the cost, subsequent cost environment. So then, recent couple of years, the high flow nasal canal therapy is coming up very meaningful, popular, okay. So the question is, the indigenous bubble, superb setup, is hardly taking hundreds in Indian rupees and versus in the high flow and other way is in lakhs to invest in the missing and consumable in thousands, couple of thousands. So we decided to compare head to head. So is it going to make any difference. The terms of treatment failure and requiring what is called non invasive ventilation, or invasive ventilation,

basically respiratory support escalation. So we randomized in the two group like one month to 23 months, presenting with moderate to severe bronchiolitis and requiring further respiratory support. One group is CPAP begins with five centimeter, maximum seven centimeter. Another group is high flow. The flow based based on the weight, titrated within at the end of 24 hours, the HFNC group found almost that failure rate is only 23% but in compared to that one, the CPAP group is almost 47%. This is really significant. And another important thing, we found that the escalation to the ventilator support, particularly non non invasive ventilated support, also significantly is lower in the HFNC group. So the one another important thing is the products in this study is the median duration of the oxygen therapy and hospital stays one day is higher in the HFNC group, but it could be due to because of the some variation in the weaning protocols. But in the study purpose, we used only FiO_2 to wean first, then flow later. So, but still, we need to study separately the weaning modality in the HFNC. I hope this one of the author in the study is planning for that one will be more answer in the future.

Traci Wolbrink *10:33*
Fantastic. And same question to you, has this changed your practice? Do you use exclusively?

Ramesh Kumar Ramachandran *10:39*
Yeah, I am for HFNC guy now, because I used to HFNC now when almost all the bronchiolitis, including post extubation, everything is HFNC making one really important modalities, preventing the intubation and ventilation. So since beginning, we are using HFNC online, yeah.

Traci Wolbrink *11:01*
All right, well now that we've heard a little bit about the studies, I want to dive a bit into the conducting of randomized control trials and some of the challenges that can be associated with doing this type of research. Now I was, I attended the pediatric research networking session yesterday, and we talked a lot about research here, the current state of research in India, and goals for the future. I was hoping to kind of start illuminating first, starting with maybe some of the challenges to doing these kinds of studies. And I think, honestly, the challenges that you face are the challenges that everybody faces around the world when trying to conduct a randomized control trial. But maybe Dr. Ashish, I could ask you, what were some of the challenges that you faced as you were trying to implement this study?

Ashish Agarwal *11:49*
Thank you, ma'am. So as we have this our trial was conducted in a resource limited setting where we have, as I have told, we operate at around 500 to 600% occupancy in both emergencies and we are very busy. Because most important challenges which we face in conducting such trials is, one is logistic issues, the resources and also the manpower issues. So just to point a couple of couple put into the study. So this study required the balance the trial fluids that is normal saline and Ringer's lactate. So the fluids, generally in resource rich countries, are supplied in collapsible bags, air free bags. But most centers in resource limited settings, the IV fluids are supplied in rigid plastic bottles which are which are non collapsible. It is very difficult to blind this fluids by wrapping the foil paper and then using them for this thing. So it was quite challenging to get those bags, or bags or so just to just to point a few, a couple. Another thing is, like we wanted to do ketones every four hours, so there is no steady supply of those ketone point of care, ketone strips. So main thing which we face challenges is the logistic issues, or the resources are limited. And in whatever limited resources we have, sometimes we have to spend from our own stipends and get these resources to conduct these trials. Also very, very important thing is the manpower. The residents, the nurses who are working in setting like us. They are, they are quite

overstretched in both their clinical responsibilities, each and in a busy emergency room, where one bed, one bed has three to four children who are critically sick, and one when nurse is looking after so many children. But most important is when we conduct such trials, we have that very good team effort. They stretch themselves beyond their responsibilities and help in conducting these trials in a smoother way, in a protocolized manner, so they help us out. So the residents who are working day in and day out, they most of the residents who are working in while doing this trials, they're working 16, 18 hours a day, helping other colleagues to conduct these trials and enroll children, collect data, so we don't have dedicated research manpower to conduct such trials ma'am. So that there are the resources are less, the manpower is less. But still, despite all this, like we try, we give or more than 100% to go beyond and collect the data in a very protocolized manner, and conduct such trials. We should love what we are doing. We should give our heart and soul so then we can stretch that extra and get out, get all the data and conduct a trial in such resource limited settings. The positive point which I see is we get a good number of cases and sicker case. Suppose diabetic ketoacidosis in developed country, they may not present in severe DK. They will not present with pH of 6.8, 6.9 as routinely they present with us, like in diabetic ketosis, most of our children present in very severe DK. Most children's in like in our trial, around three fourths of the children had a pH of less than seven at presentation. So the mean pH and around 3/4 of the children was 6.8, 6.9. So it is good that we get such load of cases and we are able to conduct such trials with the fluid, which is the main talk, which is the main debate on which type of fluid, so we have those cases, and we are able to do such trials.

Traci Wolbrink *15:26*
Well, thank you. I mean, you highlight so many things. You highlight the resource constraints, the manpower constraints, but then the fact that, you know this really is a labor of love and being passionate about it sounds like you're able to mobilize a team to work with you and be collaborative. And you know, there's a greater good that we're sort of working beyond. One other question that I had related to you, I attended and helped facilitate a workshop that Dr. Rakshay Shetty designed called SIMPACT, where we talked about the use of simulation for quality improvement. And I wonder, you know, as you were describing all the different challenges that can go wrong with your protocol, with implementing this, did you do any dry runs or practice or sort of think about running through any of those activities, you know, similar to what we might do with simulation and sort of systems testing or practicing. I'm curious how that rolled out.

Ashish Agarwal *16:18*
So a couple of months before we started, we started enrolling children. We every day we used to go around emergency and ICU. We prepared all the pamphlets and all we have displayed everything that such, such a trial is going to start, and we, all the nurses, all the resident doctors, were initially told that we are going to do this trial, and if any child of diabetic ketosis comes to emergency any time of the day, whether it's 2am, 3am, whatever time of the day, the principal investigators will be called. He is going to visit the emergency, enroll, randomize the child, enroll. So yeah, definitely all these things help we had done at this thing before starting the trial, and then we started up.

Traci Wolbrink *17:04*
Fantastic. Thank you for highlighting the the amount of work and practice and run throughs that you did in advance. Because I think when you think about a study, you think, you write the protocol, and then magic happens, and the trial begins, but there's a lot of work up front to get everything started, all right.

And now turning to you, Dr. Ramesh Kumar, I was hoping you could describe some of the challenges that you faced as you were sort of working through your study and implementing that.

Ramesh Kumar Ramachandran *17:30*
Definitely there is a logistic issues in the specific emergency room, but the previous experience, what we conducted couple of studies in the RCT, so that gained lot of knowledge and experiences. So in this study, writing protocol, and then we decided, because we are already using bubble CPAP, we are already using in HFNC. So when we have a finding for weekly review or monthly review, and what is the problem happening in this modalities, when patient is on going on care, so that is then we find out one or three things. But specific to the study, we ensure, we need to ensure the consistency in the setting up of nasal prong, and consistency in setting up of the five centimeter PEEP, then consistency in the escalating that is the very toughest one. So before studying study, so we test run, for example, around five to seven patients. So because when studies comes this all are important. So we did some test run so we find it is feasible. There's no issues, and that is helped us. And other thing is we need to consistently deliver the consumable for the high flow, because, as per ethics committee, the studies would ensure everything to the patient. So we secured the institute support, internal grant support. So that is helped us. And after completion of the studies, of course, we know that once the RCT is writing protocol is tough, but end of the day, writing manscript is not a much problem, but execution is the more important. So we found these two is very important hurdles. So from that we what we learned that so whenever we are going to plan it, so we our fine tune our writing protocol, writing skill for next RCT, because next RC is planning for meaning modality in HFNC. So we fine tune our writing skill in the protocol itself, each and every points like introduction methodology, how to deliver, and now we are put it test run in the incorporated in the protocol itself. We are going to test run this particular protocol for a couple of patients, and with prior approval from the ethics committee and all those things, it's going to help us. I hope going to help us.

Traci Wolbrink *19:51*
Fantastic. One of the things that you mentioned was trying to standardize your protocol being more exact in the way that you deliver care. And I'm curious about whether or not you think it has made a difference in the type of care that you deliver. Oftentimes, studies are great opportunities for us to change our practice and sort of get on board with different checklists and protocols and improve our care. Because we, you know, are paying really close attention to that. I'm curious if you saw any changes even beyond the study period that sort of lasted in your ICU.

Ramesh Kumar Ramachandran *20:26*
Yes, because I'm saying is, this is the residents will keep with it. Okay, so during the study period, the particular residents will be there. They are aware about the studies going on and how meticulous we are about the setting up the people, what is called CPAP level five or six, everything the subsequently we inform or we do need to train them why we need to come out, what is called teach them the new resident. Otherwise we will lose the track, because when study is there, we will pentecostally measure the scale with everything five centimeter, when study is not going okay, even approximately they can, because the resident mindset is totally different, okay. So I observed in the couple of almost six months to one year, the when we are conveying over the points to the residents, they also happy, and they learned so for me, is when we are going to deliver the care. So this study made us to fine tuning, so this would be implemented in your routine protocol, in the care. So how meticulous about your CPAP setting setting, and how meticulous about your measurement and all those things. So otherwise, we will

lose the track after six months or on a year. But I observed that couple of six months, this was fantastic, and I hope that the other author, we might continue the same.

Traci Wolbrink *21:45*
That's great. I think we often talk about how, you know, there's clinical care, there's research, but I think what you've highlighted is just the fact that research, both of you, research informs the clinical care that you then go on to deliver afterwards, and it can also make practice changes in your unit that can help deliver clinical care even better. So just the fact that participation in research can increase both of these, I think, is really exciting, and leads me a little bit to my next question, which is any advice that you have for junior trainees as they get started, or junior faculty about you know, the importance of doing research, any tips or strategies about how to get started or stick with it when it might be challenging?

Ashish Agarwal *22:31*
Yes, ma'am. So as you have rightly said, when we do research, for example, as the previous point, if I come to the previous point, my mentor, Professor Jayashree Mudiyan, so she has done most of the research in diabetic ketoacidosis. So she we have tested insulin dose, type of fluids, volume of fluids. Now in the unit, there is a set protocol. There is a standard operating protocolized care. Each junior residents also knows that if a child with DK comes, what are the steps which are to be done so, doing research consistently on a same topic, has refined that care in the unit. There is no difference in the care which the practicing physicians or the residents provide at the ground level. So each and every resident knows that if the child with diabetic ketosis comes, then these are the steps which are to be done, which are being done since a decade. Because all the all of this research, research has been done so for junior colleagues, the thing is, definitely with experience, we can say that doing research helps us to know what are, what are the challenges at the ground level, in the patient care, whatever the care which we are providing, we also come to know the challenges when we when we do research, because we want to do it as per protocol, and that time, we know that these are the things which which get missed in those busy emergencies or ICUs, and definitely it helps in refining yourself in clinical practice. So definitely, yes, but the most important thing is you should love what you are doing. So the research topic which you choose is you, you should love that. Yeah, this is the topic which I want to do. So before, before joining DM in pediatric intensive care, I always dreamt of doing some topic in fluids. I was very it was my dream to do some thesis in fluids. So and when I joined, and then when this thought came from my mentor, she said that will test type of fluid in diabetic ketosis. I felt that this was a dream come true, and then I gave my heart and soul to this research. And yeah, I'm really happy that it got recognized in an international journal, and we're able to make difference in our clinical practice.

Traci Wolbrink *24:48*
Fantastic. I think you you outlined a few things. One, being being passionate about your particular topic, one of my mentors always told me that you have to do something that really makes you want to get out of bed every morning and come into work. And so it sounds like fluid is that for you. You also mentioned the importance of mentoring. And I'm curious, how do you find a good mentor? What makes a good mentor? What are some of the things that people should be looking for in a mentor.

Ashish Agarwal *25:17*
My mentor, Dr. Jayashree Mudiyan, like, I don't have any words for her. Like, whatever I am here is all because of her, like, and also the greats which were sitting. Bansal Singh, Sir. So what they do is they

will give you a topic which you are interested in, and they will, they will not interfere. They will give you that independence of doing that research and and whenever you are in stuck in some administrative issue, logistic issues, and then they are going to help, help you out in all those problems. So obviously, yes, a good mentor is the one who recognizes that what his students loves the topic, what he or she would love to do, and then nurturing that thought and then taking it further.

Traci Wolbrink *26:08*
And for you last, any comments, words of advice for junior people that are getting started.

Ramesh Kumar Ramachandran *26:15*
The most important part is when I'm going to some particular unit, first look at the feasibility. Is it feasible to the particular study in that given unit? Number one, looking at the data, previous year data, then you can go for that further, writing up the protocols with the help of the mentors, and of course, definitely they will available for this one. And I emphasize more of the writing the protocol. Make it as perfect as possible. Okay, there, once the protocol is done, then give some test run. Then do modify again, whatever modifications. Then, once study started, stick to the protocol, try to collect the data meticulously. Then thereafter, there is no stop. Okay, whatever the result, whatever the discussion, doesn't matter. So feasibility is the top most priority for me, the given city, the given resource. So what I can do? Okay, because I can. I mean, what many wonders, but even many small, small things, even the routine clinical practice data. If you analyze properly, collect properly, it will make [difference], definitely.

Traci Wolbrink *27:21*
That's great. I think those are such important points that you have to be realistic about the research that you can conduct. What is going to be reasonable in the time frame you have, with the resources you have, with the mentors that you have, in the team that you have, and then when you bring all of that together, you can be passionate. You can start writing. You can get that out very early, is what I think I hear you...

Ramesh Kumar Ramachandran *27:43*
Yeah, because my resident, my resident, when I was resident, my RCT guided by Dr. Singh Sir when I was in fellow my again RCT, so guided by Dr. Bansal, Sir, and Singh, Sir. So really learned a lot. So they made me is, I'm one of the interest in the clinical research. I am. I love clinical research. So they guided me a lot of thing, how to go back to go get it all the steps done. So I attended many clinical research workshop and everything. So the end of the day, the protocol is everything, okay, so protocol, protocol, protocol, okay, then we can execute and other things before, okay.

Traci Wolbrink *28:27*
Well, thank you both for sharing your insights today on the, I think the first ever podcast we've done live at PEDICRITICON. So thank you for being the inaugural podcast guests, and thank you to the audience for joining us today.

Ramesh Kumar Ramachandran *28:42*
Thank you very much.

Ashish Agarwal *28:43*
Thank you. Thank you.

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