Erum Khan, MSc, FCPS, MBBS

Behind the Mask

February 23, 2024

Barr: Good morning. Today is February 23, 2024. My name is Gabrielle Barr, and I'm an Archivist at the Office of NIH History and Stetten Museum. Today I have the pleasure of speaking with Dr. Erum Khan. Dr. Khan is the Chair and Professor at the Department of Pathology and Laboratory Medicine at Aga Khan University (AKU) in Pakistan, as well as the Chair of the Institutional Biosafety Committee within the medical college. Today, she's going to be speaking about her COVID-19 research and experiences. Thank you very much for being with me today.

Khan: Thank you for having me, Gabrielle.

Barr: Absolutely. Will you please discuss your work early in the pandemic on comparing N95 respirator fit testing with commercially available and in-house reagents? What are some of your findings? Did you ever have to resort to this solution with the PPE [personal protective equipment] shortages and other supply chain issues throughout the world?

Khan: Thank you. As you know, during the early days of COVID-19, many health care workers got infected and lost their lives in the line of duty. That was the time when WHO [World Health Organization] and CDC [U.S. Centers for Disease Control and Prevention] categorically recommended use of N95 masks as part of the standard PPE. Now, those who have a science background know that when you're wearing N95, there are certain prerequisites that you need to ensure are in place so that the particular mask fits well on your face, based on the model of the mask that you're using and the make that you have in your hand. Generally, we tested by using a test called “fit testing.” This fit testing generally requires a very special kind of solution that you expose to the person to see whether they can smell or taste it while wearing the mask. If they can do that, that means the mask is not a very good fit. Then we might ask them to either use a different one or put it on in a more specific way. This was mandatory at our center when it became mandatory that all health care workers wear N95 masks. Before COVID-19, N95 was only recommended for people who are working either in biosafety level 3 labs or in specific clinical areas. But now that everyone had to wear a mask, there was huge anxiety among the staff that they had never been fit tested. They wanted to be fit tested before they could feel safe and okay to go and work. We initiated testing, and since Aga Khan University has a huge healthcare system, we had to test more than 3,000 faculty, students, nurses, and lab technologists working within the laboratories. This was a huge task. To be honest, we did not have enough of the chemicals to test them all since there was a complete lockdown and there was no supply chain. Chains were breaking down because shipments were not coming in. That was when we decided to develop our own chemical. And we did that. We luckily had very good people in our pharmacology department—including our biosafety officer, who was very proactive. We developed a solution that was a combination of saffron and sodium benzoate and compared it with a chemical that was

commercially available. The two were found to be equally effective. That's how we started using it. Otherwise, we would not have been able to do fit testing for more than 3,000 staff and faculty members. This was a huge success. It also saved us a fortune since we stopped importing it once we had our own.

Barr: Three thousand! That's a huge number.

Khan: Oh, absolutely.

Barr: Will you talk about the PCR-based microneutralization assay used to isolate the viral neutralization titers of serum from SARS-CoV-2 infected individuals, and the importance of having this assay in testing the antiviral activity of serum antibodies for the investigation of both disease-driven and vaccine-induced responses?

Khan: This was an interesting study that we did. I'm basically an arboviral virologist. My basic interest has always been on various arboviruses. In Pakistan, we see lot of dengue, and then there are other viruses like West Nile. Most of these viruses have antibodies which cross react, so if someone was infected with dengue virus, and I tested against West Nile virus, it may cross react with it as well. To prove whether this is truly dengue or truly West Nile, we had to develop a test, which would be a gold standard test called “plaque reduction neutralization assays,” or PRNTs. Since we already had the existing capacity to not only develop those tests, but also to assess and interpret , when COVID hit it became very important to see the people who were getting vaccinated and whether the antibodies they are developing are truly neutralizing virus or not—so that we could tell them if they are immune and good to go. This PRNT test actually takes a longer time and also requires a biosafety level 3 lab, which is a specialized kind of lab. We wanted to make sure this new assay could be done much quicker to minimize the need for incubating viral cell cultures for a longer time and to reduce the risk of exposure. We brought in a PCR-based assay. Instead of looking at neutralization from the plaque development point of view, we started looking at doing the PCR after incubation and monitoring the CT values. This was a very exciting moment for us—to see what we could monitor by lowering or increasing the CT value telling us the patient sample has antibodies, which are actually neutralizing virus. That is something that we developed that got published in PLOS ONE journal, which is one of the very good journals, and we were very happy about it. We are continuing to work on it, trying to improve this assay and make it even better. It had two impacts—one, we were quicker to respond to people and, secondly, we did not need to work in a BSL 3 lab for a long time—so both the exposure risks and the turnaround time was improved. That was a good thing.

Barr: That is a really good thing. Will you also discuss your role in the observational study conducted between October 2020 and May of 2021 that looked at how humoral and T cell responses to SARS-CoV-2 revealed insight into immunity during the early pandemic period in Pakistan? That was a really big study.

Khan: When COVID initially hit, there were a lot of assumptions, especially for LMICs [low- and middle-income countries] and countries like Pakistan, which has a huge population and high density. The risk for cross transmission and the possibility of morbidity and mortality would be very high, because people live in very congested and very closed areas. Transmission would be high so the risks would be high. But it turned out that morbidity and mortality wasn't that high. We started seeing people who were infected, but someone who was

living with that person was not getting infected or not getting very sick. As microbiologists and as immunologists, it occurred to us that maybe there are some antibodies or some underlying immune system which is protective of these patients who are not the patients, but the healthy controls—or the people who are living with the infected person. That was the main reason triggering this study. We wanted to see both the antibody-based responses—which is called the humoral response—and the T cell-based responses, to see if the patients who are getting infected had some kind of a previous protection, or if they were just naive and they all got exposed.

We started looking at the antibodies against two antigens of the virus itself, primarily focusing on the spike antigen because that was the neutralizing agent. We compared it in both, the healthy controls and the infected population. At the same time, because of our previous research, we also had some archived samples from people before COVID hit—research work that we did in 2017 and 2018. We pulled out those samples as well to see if there were any baseline antibodies that were there. To our surprise, we did see some activity—we did see some antibody that was reacting. The antibodies were cross-reacting with SARS-CoV-2's spike antigen. That gave us an inference that possibly there were some cross-reactive, anti-reactive immune responses both for the T cells as well as for the antibodies that existed. Now, whether this was in response to closely linked other respiratory viruses, which are common in Pakistan—that needs to be explored further. But this study definitely helped us in identifying that the population of Pakistan, because they live in a very close and congested area, whenever the respiratory outbreaks are there—whether it is influenza, SARS-CoV-2, or RSV—then people do get exposed, and this is sort of like a natural immunization. The herd immunization concept comes in over here. It was also protective for the larger population. Luckily, because of this herd immunity, we did not see as high morbidity and mortality as the rest of the world.

Barr: Are you working to see the responses across the different variants?

Khan: Oh, yes, in the future. Initially, the only variant of interest at that time was Delta. But we are looking at trying to develop more studies in the future, where we could see the impact on individuals. But the only challenge that we had was getting samples from healthy people. At that time, if you remember, there was a lot of fear of COVID-related restrictions if they were found to be positive. They thought that we were screening them to see if they were positive, and then there might be some restrictions applied to them. But luckily, we did manage much of it, and we did publish this study—that I'm really proud of—in BMC Infectious Diseases.

Barr: Did you see similar results amongst the different regions of Pakistan?

Khan: Yes, of course. Region-wise, the new study is in the planning process and waiting for the grants to come in. It is targeted on the different variants that we see and also the site of origin from where they are coming in. We will be mapping it out based on the data that we already have. Then, based on those regional areas, we will be going in and exploring further the responses to these variants to see if any particular variant had more response than the others. Yes, we are planning that.

Barr: That will be really fascinating. Will you please introduce your perspective observational study that looked at the impact of prior COVID-19 Ig [immunoglobulin] antibody and interferon responses after [Sinopharm's] BBIBP-CorV vaccination in a disease endemic population from April through October of 2021, including how you and your colleagues went about planning and conducting this study?

Khan: This study was, again, part of our larger group. We had a big team that was looking at those various immune responses. One of the major people who was involved in this was Dr. Zahra Hasan, who's also a world-renowned immunologist. We tried to look at what kind of responses these patients were developing, and the interferon responses as well. We developed a very specialized assay to help us identify this, and we primarily looked at the IgG seropositivity against the spike. This time, we added another small antigen component of the virus, which is called RBT. Those were the two proteins—RBT as well as a spike. We tried to look at it from the point of view of how it would be beneficial to see what kind of a vaccine response is more effective in our population. During those early COVID-19 days we had vaccines from all over the world as donations. They came in from Pfizer, Sinopharm—many different commercial vaccines came in. We wanted to see which vaccine was effectively helping develop the neutralization or protection of the population or the patients. That was a very, very important study for us. We looked at the responses of those who were given these vaccinations, then we followed them for up to 24 weeks. Based on that, after 24 weeks of vaccination, we took their samples again. We compared the T cell responses as well as the IgG responses to see how this is helping them, or if they are responding to the vaccines or not responding to the vaccines. This was a very good study. We're trying to follow these patients for even longer in the future to see if the results that we got at 24 weeks are still reliable enough for further follow-ups in future. That's what we did in the coronavirus BBI vaccination study.

Barr: Will you share a little bit about why your place of work, the Department of Pathology and Laboratory Medicine at Aga Khan University, was prepared to handle the challenges that COVID-19 presented, such as its expertise in genome sequencing? Can you speak a little bit about some of the collaborative research you and your coworkers engaged in beyond the papers we discussed, and some of the entities you are partnered with?

Khan: Sure, absolutely. The Department of Pathology and Laboratory Medicine at Aga Khan University is very much driven both by high service standards and also by the research work that we do. Aga Khan University primarily has a mission based on an acronym called IQRA—impact, quality, relevance, and access. That is what we follow, and because of that, we try to do research that has an impact on our local population. Then whatever translates out of it, we can apply onto the population—whether it is in the form of a policy or development of a new test. That's the thrust of the research. I'm very lucky, happy, and proud to say that Aga Khan University has always been very, very facilitative when it comes to research. It has a huge research mandate, and it has invested heavily in research. AKU has very well established, fully equipped laboratories that can assist us in doing research work. These are, dedicated research labs and not the clinical labs, so we are able to do that work over there. Plus, we have systems in place where we can administer large grants, so that the finance team and the HR teams are out there to help us. That's why we have a very good research portfolio maintained within the department.

The reason we were able to quickly switch to developing new tests for COVID-19, or to assist the government in doing a large number of tests, was that we already had a lot of research going on. When COVID-19 hit, there wasn't much capacity for testing samples at a national level. Aga Khan University was asked by the government to help in doing those tests and upscaling our throughput for COVID-19 testing. But to be honest, clinical labs did not have enough human resources to handle those large numbers. The research capacity came in handy. We already had people who were very well trained in terms of doing molecular testing, doing genomic analysis, interpreting the genomic data, and handling highly sophisticated equipment like NGS [next-generation sequencing], so we bridged that service gap. As wall the research teams came together. It was kind of a synergistic effect. We had times when we were doing more than 1,000 tests a day and reporting those out in a very short turnaround time. That was a challenge because government wanted active reporting and we were working 24/7. There were no breaks. If we did not have the research capacity already there, this might not have been possible for us to do. We are very thankful to the collaborative international entities that we've been working with for quite some time. These included Fogarty International, who came forward very early in the course of the pandemic when we reached out to them. They were already collaborating with us on other projects, but they helped us in terms of protocol optimization and exchange of the agents and controls. We have also collaborated with CDC USA on various other project—so we reached out to them early—and we also had already established links with WHO Pakistan and Bill Gates. There are currently active projects going on with the Center for Research in Emerging Infectious Diseases—the CREID—at NIH, and the United World Antiviral Research Network (UWARN) that is in collaboration with University of Washington. These were the entities that we were already working with on other research projects. When COVID hit, we all came together and centrally focused on COVID so that we could quickly turn things around, develop the tests, help government agencies, and protect the community by quicker application.

Barr: There are many positives, but what were some of the challenges that your department experienced during the pandemic, and what do you feel like you've learned from all of your experiences during this very dynamic time?

Khan: The biggest challenge, and I believe this was for everyone, was the breakdown in shipment and supply chain of the kits and reagents that we use. That was the biggest challenge. Air travel was stopped, and sea travel was also affected. The supply chain was disrupted very badly. That was our biggest challenge. The second most important challenge was the optimization—the speed with which we were to optimize the assays. The variants of interest were changing very fast, so we had to quickly adapt ourselves to be able to test changing variant. In Pakistan, we did not have a very big government-based agency where people could send their assays for confirmation, so most of confirmatory tests were coming back to AKU. We were becoming like the de facto reference lab. We were confirming other lab tests as well, so that was overwhelming.

Barr: That's a huge responsibility!

Khan: That became a really big challenge for us—We wanted to help them validate their own assays and help government validate kits that they planned to procure for testing Pakistani Population. But then, of course, that's the role of the academic center, and we did play our role.

Barr: Were you the person in charge of organizing how all the testing of all these different samples would be carried out?

Khan: At that point in time, in 2019, I was not the Chair of the Department of Pathology. I became the Chair of the Department of Pathology and Laboratory Medicine in 2022. But yes, before that, I was primarily involved in the diagnostic and research side as a faculty member. We were part of those coordinating activities and working together.

Barr: How did you keep up morale with going 24/7 and having the responsibility of testing for your whole country?

Khan: Yes, that was a huge challenge, keeping up and motivating the technical staff and faculty members, as well as the administrative staff, because we needed everyone to be around while we were working 24/7. We also rotated them, and that was a good thing. We had the research side at hand helping us in that. Also, I must say that the technical staff were getting infected—from the community because the disease was progressing in the community. We were facing a huge shortage of human resources in almost every section. But we kept talking to them, communicating with them, meeting with them on a regular basis, and letting them know how we are helping them and what excellent work that they were doing. That kept the morale high. Otherwise, it was quite challenging.

Barr: You spoke a little bit about how you wanted to expand some of the work that you've already done, but what are some of the other COVID-19 initiatives or studies that you hope to be a part of?

Khan: As I mentioned already, we are trying to look at the immune responses to various vaccinations. Also, we would like to look at long COVID to see if there are any elements that we can link it to, because it is becoming very difficult to differentiate whether the Long COVID is because of the primary disease itself or if the vaccine has any impact on it, and if it is linked to any specific vaccine outcomes. Those are the kinds of interesting questions that we have in mind and would really like to look at in the future.

Barr: Can you talk a little bit about how your background with dengue frames how you have looked at SARS-CoV-2?

Khan: My background in dengue and other arboviruses really helped me in developing these new assays. As I mentioned earlier, I worked with PRNTs [plaque reduction neutralization tests]. After giving the vaccine, or even before, we wanted to see why the mortalities are not high in Pakistan. The first thing we needed to look at was the neutralization assays. I had this background because of my prior work with the arboviruses. That really helped me in putting my efforts towards this pandemic work that we did together in collaboration with other departments at AKU. That was my role, and I'm really happy that I knew all those techniques so that I could help.

Barr: You mentioned that you've worked with the Fogarty International Center for many years. Can you talk a little bit about how your association with them influenced how you and others at Aga Khan University approached the pandemic?

Khan: Oh, yeah. Fogarty International has been very active research collaborator in Pakistan in different areas. Our association has been at the diagnostic lab level. As well, they have done tremendous work on biosafety capacity building in Pakistan. Also, even before COVID-19, they conducted a lot of workshops in Pakistan involving genomic studies, looking at various pathogens and keeping in mind how genomic data can be analyzed if there is an outbreak situation or other hypothetical situation. All those workshops had been there in the past before the COVID-19 epidemic. Specifically, when it comes to research and diagnostics, we had worked with Fogarty International on various projects like salmonella typhi—multidrug resistant salmonella typhi is very common in Pakistan—and tuberculosis linked projects. We were also engaged with them on cholera isolates that had an epidemic outbreak in Pakistan. From time to time, Fogarty has been very forthcoming in helping us solve cases where we are unable to diagnose or when there is an outbreak situation, and we need urgent reagents and supplies. They've been very kind. Fogarty was definitely the go-to center when it came to COVID-19. We were really lucky to have them on board. We were the first one to report COVID-19 from Pakistan—because they helped us optimize the assay, they shared some agents that we didn't have, and also shared the control. That was an excellent collaborative function that we had together. You asked earlier what I learned from this pandemic. Through this, we learned that this collaboration that we already had gave us speed to our work, and what I learned is that speed is the game changer. The earlier you knew, the earlier you could develop the test, and that is how you would put a lid on this pandemic. Even for the future, that is something that we, as scientists and as a community, have to be working towards—how we can work collaboratively—so that if there is a new potential epidemic outbreak in Pakistan, we are quickly there to respond to it and to inform, and others can quickly help us.

Barr: In addition to being a researcher, you're also an individual who's lived through the pandemic. What were some of the personal opportunities and difficulties that COVID-19 presented for you?

Khan: Oh, so at the personal level, of course, those times were very challenging. I had one very senior citizen living in my house, my mother-in-law, who was also a cancer patient. My husband is also a healthcare worker, so it was very challenging for us coming to work and then not taking the bug back home. That was a very critical time for us. We didn't want to leave her alone, because for the senior citizen, that kind of environment also creates a lot of anxiety. We kept connected, but yet it was very difficult because she was living with us. That was a challenge at a personal level. Then my son was away at university outside of Pakistan, and borders were closing. Getting him from Malaysia back to Pakistan was a challenge. At a personal level, those were the challenges. But I learned a great deal during this pandemic from how the community came together. Everyone wanted to give you a helping hand: "If your mother-in-law is ill, we can give her food, don't worry about that. Stay in your office if you have to." We were working in the lab 24/7 sometimes. I used to stay back in the lab until 2:00 or 3:00 in the morning. Those were the times I was really concerned about who was going to take care of her. Neighbors and other people came in to help, so that was the kind of community mobilization we saw at that time. It was really good. We also learned how active public-private partnerships were really helpful. Aga

Khan University also supported health commissions in Pakistan. In Pakistan, the health is managed at provincial levels. Sindh Health Care Commission and Punjab Healthcare Commission approached us for various things they wanted us to help them with. Not just reporting, of course. We were reporting every day, but they also wanted us to help them in terms of validating laboratory kits for them. And we developed a center for vaccinating everyone at Aga Khan. Those were the things that we helped with, so both public and private sectors came together very actively. That was a huge learning experience as well. We helped develop various protocols for how to make PPE, how to wear PPE, and how to remove PPE in the lab. That was a big lesson for us.

Barr: Definitely. How did you continue teaching during this time?

Khan: For teaching during COVID-19, we had to go from in-person teaching to online teaching. That was a huge challenge for us, because we were not geared and tuned in that way. Both students as well as the faculty adapted very well. Most of our teaching and training went to online modules and courses. This was a blessing in disguise. While we didn't like it being online and we wanted it to be more in person, at the same time we were able to open our teaching modules to not only students within Aga Khan, but all over Pakistan. And that became a huge success, because people from all over Pakistan wanted to learn how to put on and take off PPE. People from all over Pakistan were trained on how to collect samples. We did these online courses and we had as many as 6,000 attendees at one time. Our system crashed, actually, so we were not able to continue with that. We tried to do multiple sessions rather than have one session. That was a huge opportunity, and we continue to do so. We have developed this VLE [virtual learning environment] module where we put videos because there was huge demand. People really wanted to have information about COVID-19, be it lab test diagnostics or clinical site management, and especially anesthesia management. Yes, Aga Khan University definitely came out shining by teaching the entire country about COVID-19 related things.

Barr: Is there anything else that you'd like to add about your COVID-19 research or experiences?

Khan: One more thing that I would like to express here is that taking these lessons from COVID-19 forward, I think one of the biggest things that I have learned, or where my knowledge has improved, is that success lies in having a very successful team. The team has to be as broad-based as it can. Not just the scientists, but we also need people who are administrators. And we need people who are good communicators to communicate with the community and societies. One of the challenges that we felt during COVID-19 was a lot of disinformation that was circulating at that time. No matter what we as scientists were telling them, they kept saying, “Oh, no, no, they are making it up.” A lot of the false information was circulating at the early hours. Now that we have learned this, every country should have their own team building, so that they have communicators, and they can constantly educate their communities about various information—because that is the minimum. The community knows a lot about politics, but they don't know about their own infections that can kill them. That is something that we have to make sure of. Also, what I learned from this is that dependency on international imports for LMICs like Pakistan is something detrimental. We need to be self-sufficient or at least have local or regional agencies where we can develop our own resources from within. Relying on our own resources would be something that will help us in the future as well. That is something that I would like to express.

Barr: Well, thank you so much for interviewing, and I wish you and your whole team continued success in all that you do.

Khan: Thank you so much for having me. It was really a pleasure talking to you.

Barr: Thank you.

Khan: Thank you.

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