

AKI and the Global Burden of Disease

Jorge Cerda, MD, FACP, FASN

- Speaker 1: [00:00](#) I would like to introduce my colleague and friend, Professor Cerda who will talk about AKI and the global burden of disease. Professor Cerda.
- Speaker 2: [00:18](#) It is my pleasure again to be part of this wonderful meeting and I enormously appreciate the invitation to share some data with you. In the limited time that I have, I will describe the way we see the global burden of disease with an emphasis in low and middle income countries, because we think that the global burden of acute kidney injury is more than epidemiology and it has to do with a human burden of disease and the acute burden in the world has to do with the disease itself as well as with a context. You would not be able to understand acute kidney injury in developing world without understanding the availability of clean water, prevalent endemic diseases, maternal and child health, etc. And, at the turn of the century, the United Nations came up with the Millennium Project. And, those were the goals.
- Speaker 2: [01:19](#) So what was needed to be achieved as an International effort. And if you see, most of the goals have a lot to do with acute kidney injury, maternal health, protection of children, and the the diseases that have a severe impact on acute kidney injury such as malaria. In low middle income countries. Acute kidney disease is a disease of the young, discrimination plays a significant role, major endemic conditions lead to acute kidney injury, and as I said, poor maternal health including abortion, preeclampsia lead to severe acute kidney injury. The subsequent Millennium Goals, the sustainable development goals, again emphasize the same relationship and in this, the presence of endemic disease play a central role in the immunology of acute kidney injury because the development of acute kidney injury has to do with the individual, but this individual in the context, it would not be possible to understand it without considering social factors, geographic and economic factors that not only determine the onset of acute kidney injury, but also determine the outcome.
- Speaker 2: [02:31](#) So the key points I will try to make is that in low and middle income countries, acute kidney injury is increasing rapidly. Part of that, as I will briefly mention, has to do with better ascertainment undoubtedly, but also there seems to be a real

increase, but there is uncertainty and the true incidence and that uncertainty, limits awareness and reduces this political visibility. And as a result, very little is done about it. And importantly, acute kidney injury leads to chronic kidney disease in many cases. And this is a dramatic problem in developing countries because those are the countries that cannot afford to manage a chronic kidney disease and end stage renal disease. So the other point to make is that acute kidney injury can be prevented and nowhere this is more evident than in the developing countries where prevention is the way to go.

Speaker 2: [03:24](#)

And prevention can achieve enormous improvement because if you look at the natural history of acute kidney injury, we tend to focus on kidney failure and death. But we need to look for ways in which we can revert the process and bring the patient to health or as much health as possible. So, trying to assess the burden of acute kidney injury. A few years ago we did meta-analysis as part of the, AKI Advisory Board of the American Society of Nephrology and that included 49 million subjects, and in that study that unfortunately was based on the literature that was available then, most of the information came from north of the equator and only seven percent came from south of the equator. But even then, what we found in these 50 million cohort is that one in five adults and one in three children experience acute kidney injury Worldwide during that interval. And most of the studies were coming from, the United States and Canada where 5% percent of the population lives while only two studies from Africa where 15 percent of the World population lives.

Speaker 2: [04:37](#)

So very few studies. And then a subsequent reevaluation that we included in an article in the Lancet. We looked at a larger population, including this time, 77 million subjects with 266 studies using KDIGO equivalent, which is a significant point in that up till then we were thinking that especially in Africa, the use of KDIGO criteria for the definition of acute kidney injury would be very unlikely and yet as you can see, multiple studies from Africa, began to appear. And then we found a series of issues that I will not belabor except for two points when we looked at the incidence and the mortality of acute kidney injury and correlated that by country income, we found that consistently, number one, the incidence of acute kidney injury in low middle income countries is similar to the incidents in developed countries.

Speaker 2: [05:35](#)

So you need to do away with the concept that acute kidney injury is far less common in Africa than in upstate New York, is not, is the same and probably more prevalent. And secondly,

the second point is that opposite to the general perception that this disease is not so deadly in developing countries, the opposite is true. The mortality of acute kidney injury is high here in developing countries as opposed to that in the developed World. And more importantly, when we correlated the incidence and the outcomes and the mortality of acute kidney injury and correlated that with the investment in health, which is a better measure of the country income, we found consistently that higher investment in health led to lesser mortality, so the message is clear, is prevalent, is very important, is deadly, but stuff can be done. And then as will be described by Etienne Macedo in a little minute in the global snapshot in which we obtained data from many regions in the World.

Speaker 2: [06:40](#)

We obtained data from both adults and children. I won't be labeled on that because I will be wonderfully described by Etienne except for the data on children and this will be published soon in PLOS ONE, in which we found again that mortality by income regional location shows that the mortality when you compare high income with low and middle income, you can see the dramatic difference, in all the issues. And the second issue is that when you compare rich countries with poor countries, the incidence of community acquired acute kidney injury is extremely prevalent. And when you importantly look at mortality and derive the adjusted odds ratio of death, the odds ratio of this if you are a child in a developing country is 17 times higher than the mortality in high income countries. So the message is clear, right? And that is across all degrees of pRIFLE criteria as well as whether the patients do or do not require renal replacement therapies.

Speaker 2: [07:53](#)

So part of the effort, not only needs to be an epidemiological effort, but also we need to make an effort to correlate acute kidney injury with a context and with other diseases that occur at the same time because acute kidney injury doesn't happen in isolation. And we thought in this is our effort currently, that if we incorporate acute kidney injury in the global burden of disease, we are going to be able to better describe the mechanisms, the interactions and what can be done. The Global Burden of Disease is a project that systematically, describes epidemiology and this is a very collaborative effort by many persons, around the world. And the goals of the GBD is to obtain global descriptive, epidemiology to quantitate and that is a point, a comparative magnitude of health loss due to disease injury and risk factors and for decision makers, the main idea is that they will get the big picture and they will say, Okay, this is the incidence of acute kidney injury.

Speaker 2: [09:00](#) This is the relationship with malaria. Maybe if we impact on malaria, then we will be more successful in achieving good results. So the GBD has an output that includes regular estimates of all cause mortality, death by cause, but also importantly, not just deaths, but also the years of life lost to premature mortality and the years lived with disability as well as the disability adjusted life years. So, those are the points and of course the data is processed in an enormously complex machine system that I won't even try to describe to you. It is very obscure, but the output seems to be real. And the output looks like this, in that if you are the president of a small country in South America, you have all the data that pertain to all the main diseases and you get the green if you are Okay and you get the red if you're not Okay. Then, that information is described by regions and importantly not only this is displayed by geography but also is displayed by gender for instance.

Speaker 2: [10:10](#) So the problem of malaria may be different if you are looking at girls than if you're looking at boys. And also importantly, the output permits each person to see, Okay, this is where we were with mortality in malaria in my country last year and it looks like that we're doing well because the mortality has diminished. And this gives us an enormous political visibility because everybody sees this. And if you are the president of a small country in Africa, you are going to be upset if your mortality is actually going up or down and maybe you will do something about it. So in generally the data suggested by social demographic index, that has to do not only with income but also with other very interesting variables including educational attainment and fertility and of course the higher SDI is associated with better social situation and as you can see, when you look at years of life lost, as the decreases for each disease in this case, diarrhea, you can see that the years of life lost, increase progressively, and if you look at a years lost to disease, also the same thing as, is the ID decreases so thus the impact of diarrhea or malaria. We are at the very early stages of the point.

Speaker 2: [11:33](#) This is, an example of how we are trying to process the data. This is extremely raw mortality data obtained from vital registration, so that is associated with a lot of problems with this data, that needs to be further analyzed. But I thought that I would share with you some of the issues, the data needs to be adjusted for differences in completeness across nations. They may be a difference in geography. Differences in what we attribute death to. And I think that that is a critical point in this report, but nevertheless, when we tightened the definition of acute kidney injury and then we compared 2005 with 2000, 2010 by age, as you can see, predictably the death, the

mortality associated with acute kidney injury increases with age. But when we express that as percent of all days, we found that the results are interesting, perhaps it means something in that not only the mortality increases in the later ages, but there seems to be sort of a peak early in adolescence that needs to be looked at further.

Speaker 2: [12:40](#)

And the other issue too, is that when you separate by regions, for instance, here on the right in yellow, the data on China, the mortality by acute kidney injury appears infinitesimal and that is clearly do more to a lack of ascertainment than to real data. As shown, for instance, by Dr Liang recently showing that nonrecognition of acute kidney injury in China is approximately 74 percent. In other words, for three fourths of all acute kidney injury in China is not recognized. So we have a problem, China is leading the effort in improving the situation, so more information on that later on. So the main goals are that we are going to prepare a manuscript describing patterns of vital registration and coding for acute kidney injury deaths, develop a strategy to incorporate acute kidney injury until the GBD. This has not been a simple effort. We are competing with many other diseases.

Speaker 2: [13:41](#)

Those who deal with deaths due to congestive heart failure for instance this year were able to put it in and that led us not to be able to. But we will keep on trying because we are convinced that this will improve. We don't know when and if acute kidney injury causes death, so it will be essential to begin by defining, does acute kidney injury caused death? What is it mainly associated with death and what are the mechanisms and perhaps a deal with the issue that perhaps acute kidney injury is an intermediate in the process to death and better describe that with an enormous database. So the goal is that within the Oby25 initiative, nobody should die of preventable and treatable acute kidney injury by 2025. That is a very reached goal and I think that knowing better about the burden of disease will have a significant impact. Thank you very much.

Speaker 2: [14:48](#)

Thank you very much for your fantastic review.

Speaker 4: [14:52](#)

we have one minute for maybe one question. So any question from the audience, maybe I could ask you one question. You obviously now know what's going on across the World. If you could implement one measure, what do you think would be the most important measure to improve the plight?

Speaker 2: [15:14](#)

Definitely. I think that , the main measure would be earlier recognition because if you invest \$1 in diminishing the mortality

in the ICU in the United States, you probably will reach very insignificant effort. One dollar can go very, very far in diarrhea correction of rehydration. So I think that the impact is early and then see if there is a clear problem in recognition. So I think that if we can achieve recognition and organize implementation that is enough, Etienne will describe efforts in that direction are being done now.

Speaker 4:

[15:52](#)

Thank you very much fantastic talk.