Antimicrobial resistance: A round table discussion on the “One Health” concept from the Gulf Cooperation Council Countries. Part One: A focus on Leadership

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A B S T R A C T

The threat of Antimicrobial Resistance (AMR) has attracted the highest level of attention after the United Nation (UN) General Assembly's High Level meeting on AMR in 2016. During that meeting a temporary committee, the inter agency coordination group (IACG) [1] was formulated, under the chairmanship of the Director General of the World Health Organization (DG-WHO) and the UN Deputy Secretary General. The IACG group was tasked to link, guide and advise on political steps needed to address and mitigate the emergence of AMR globally [2]. Efforts to combat AMR, however, have previously been developed prior to this initiative by several decades. Yet, the emergence of resistance continues to be on the rise. The Gulf Cooperation Council Center for Infection Control (GCC-IC) was established in 2005 and has made major efforts to address all aspects related to human infection control in the member countries. Many of which have been reached. In 2015, the board was able to draft through its multidisciplinary meeting the first roadmap for the countries on this issue [3]. Two years later a follow-up meeting took place in Riyadh on April 2017. Regional and international experts joined in to share and contribute to the understanding of AMR and to advise on further steps needed for this initiative. We dedicated 3 papers on this meeting. The first paper is to provide an update on progress form the GCC countries and further steps that need to be taken, (in press). The second paper is part one out of two round table discussions. The first round table discussion paper, which is the current paper, addresses AMR and the “One Health” concept with a focus on leadership. The second round table discussion paper addresses AMR and the “One Health” concept with a focus on human health [4].

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Dr. Hanan Balkhy welcomed the distinguished group of guests and the audience who are major partners and leaders in antimicrobial resistance (AMR) globally and regionally who have accepted to participate in this roundtable discussion.

The distinguished participants are:
Dr. Hamad A. Albatshan: Deputy Minister, Ministry of Environment, Water, and Agriculture, Riyadh, Saudi Arabia

Dr. Awa Aidara-Kane: Coordinator, Foodborne and Zoonoses, Lead World Health Organization Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR), WHO, Geneva, Switzerland

Elisabeth Erlacher-Vindel: Head of Sciences and New Technologies Department, World Organisation for Animal Health (OIE), Paris, France

Dr. Abdelaleh M. Alhawsawi: Director General, Saudi Patient Safety Center, Riyadh, Saudi Arabia.

Introduction by Dr. Balkhy

Dr. Balkhy welcomed the audience and the respected guests. She declared that the roundtable discussion will be transcribed and published as a document to the efforts of the region in combating AMR and the international engagement taking place.

Dr. Balkhy: The topic of AMR has politically engaged worldwide leaders and institutions. To mention a few, the World Health Organization (WHO), the US Centers for Disease Control (CDC) [6], the European Centers for Disease control (ECDC), World Organization for Animal Health (OIE), Food and Agriculture Organization (FAO) and many others have given AMR a top political health priority, not to mention the most recently created ad hoc group the IACG. Evaluating the management and control of antimicrobials has been integral to many auditing and evaluation tools; such as the International Health Regulations (IHRs) by the WHO [5,6], the Global Health Security Agenda (GSHA) [7], and most of the hospital accreditation bodies. It has been noticed that over the past few decades we have increasing rates of multiresistant organisms (MDROs) in our patients. So why is this happening and what can we do to slow this process down, is the reason why we are here today. The DG-WHO mentioned that the use of antibiotics in the animal and agriculture world is much more significant than in the human world and has led to increasing resistant patterns in the animal food sector [8]. The misuse of antimicrobials is also an issue in the human sector. Today under the “One Health” approach we will discuss the issues related to the emergence of AMR and ways to suppress this emergence with its relevance to both human and animal health.

Dr. Balkhy: We will start our discussion today by asking Dr. Aidara-Kane, whom I have been working with closely for the past 10 years; Dr Aidara-Kane what is the burden of antimicrobial resistance (AMR), specifically, in the food sector?

Dr. Aidara-Kane: Unfortunately, the burden of AMR is not decreasing. It is increasing day by day and some figures are quite alarming. It has been widely known that antimicrobial resistance is associated with the use of antimicrobials in humans. What remains unknown is that human health is also threatened by the use of antimicrobials in other sectors such as in animals. Antimicrobial resistance results will be antimicrobial resistance everywhere – antimicrobial resistance in one sector is antimicrobial resistance in all sectors – which means technically that antimicrobial resistance needs a “One Health” holistic approach. Humans can be exposed to antimicrobial resistant bacteria due to antimicrobial agents used in animals leading to the selection of-resistant bacteria that can be transmitted to humans through the food chain. Unfortunately, the same classes of antimicrobials are used in humans and in animals. Some of the antimicrobials that are used as the last resort for human medicine and we wish to preserve are being used in animals, including for non-therapeutic reasons; the best example for this is colistin, classified as Highest Priority Critically Important Antimicrobials by WHO [9], is being used in some countries for growth promotion. Antimicrobials are used to treat animals, just as they are used in humans; more questionable is the use of antimicrobial agents for routine prevention and growth-promotion. However, this may cause problems for the human health aspect and may theoretically lead selection and transmission of resistant zoonotic bacteria such as Salmonella and Campylobacter. As much as 90% of non-typhoid Salmonella and or Campylobacter are transmitted to humans through the food chain [9]. Hence, the food chain plays an important role in the transmission of resistant bacteria and transmission of multidrug resistant bacteria. Unfortunately, not all efforts done on the human side to restrict the use of antimicrobials are paralleled by that on the animal side because of a lack of awareness. That is something that we understood from the WHO and also from our tripartite colleagues; the World Organization for Animal Health (OIE) and Food and Agriculture Organization of the United Nations (FAO). We are working together to reduce the burden of antimicrobial resistance from the food chain. We do understand that the best way to reduce the burden of AMR is to reduce the need for antimicrobials. First, through improved biosecurity and good animal husbandry, we would be heading towards much less use of antimicrobials in animals. Second, if we have to use them, we should avoid antimicrobials that are critically important for human health, and the WHO has defined such a list among them are quinolones, 3rd, 4th and 5th generation cephalosporin; and recently, colistin has been added [10]. On the other hand, some of the critical antimicrobials for human health are used regularly for growth promotion, which the WHO does not support nor recommends. I believe Dr. Erlacher-Vindel will discuss this in a little bit.

Dr. Balkhy: Thank you Dr. Aidara-Kane, that was a great highlight of the emergence of multidrug resistant pathogens in animal food and best ways to tackle the problem. The question now is to Dr. Erlacher-Vindel. What is the burden leading to multidrug resistant organisms in animals?

Dr. Erlacher-Vindel: As veterinarians we have a much bigger and difficult challenge from those dealing with human health. As we deal with many species of various behaviors and needs, there is no one solution for all the problems pertaining to the use or even the misuse of antimicrobial agents. There are so many differences from chicken to cow, and a cow from Sri Lanka to a cow from Belgium. Therefore, the complexity from the animal side is probably bigger than the human side. Healthcare settings for humans may be easy to monitor, while we do not have such settings for animals. The second important point is that resistance among human pathogens is not common knowledge to the veterinarians. That is because there is a lack of a common platform to share such knowledge. Simply stated, many veterinarians are not aware of the emergence of AMR in human health nor are they aware that the misuse of these agents impact human health. The burden of resistance in the veterinary world should be assessed by species, which is far more difficult, and we do not have a clear picture of what that may be.

Dr. Balkhy: Those are very important points for us to understand, so what are some of the OIE initiatives to tackle these issue?

Dr. Erlacher-Vindel: The OIE is working on this issue and we have studies on the animal side that would be very interesting. As an overview, we have started to collect data on the use of antimicrobials in animals in collaboration with our 182 Member Countries. For example, baseline data are collected from the veterinary side to see what agents are being used, and for what indication, and as Dr. Aidara-Kane said, whether it is used for growth promotion or not. In the AMR Global Action Plan (GAP) [11] there is a common agreement to phase out the use of antimicrobials for growth promotion in the absence of risk analysis. All agencies and all organizations
agree on this. We are attempting to understand what antimicrobial agents are used and how much is used in each country for growth promotion. Additionally, we try to do this every year to measure global trends.

Bottom line, animals and food animals in particular are important for a country’s economy and are a major source of nutrition, so veterinarians need to treat animals; the challenge remains that this treatment takes place in a very different way than humans. In a fish farm for example, all fish are treated as communities and not treated as a single fish, which is not easy, but it is the reality since we do not treat them one by one. On growth promotion, we need to cut certain practices, especially in developing countries. Such countries may be terrified of such changes, as they fear the negative economic impact. Additional, there is an overwhelming need for education. I will repeat the 4 critical elements mentioned by Dr. Aidara-Kane, because it will be the same: prevention, prescription, monitoring, and development of new tools. Prevention: in terms of good animal practice and hygiene, use of vaccines and specifically improving the housing conditions of animals. Prescription: of antibiotics needs to be based on the diagnosis of a competent veterinarian. Monitoring: the use of antimicrobials among animals qualitative and quantitative is what we have already initiated and we have quite interesting results to share in the near future. Development of new tools: especially vaccines for animals need to be supported. We do not believe there will be a surge of new antimicrobials in the nearby future, but we believe that the future will be for the development of alternatives to antibiotics and vaccines that may control the diseases by species, resulting in less usage or need of antibiotics.

Dr. Balkhy: Thank you Dr. Erlacher-Vindel for this great summary of a very challenging aspect of AMR. One of the major eye openers for me when I joined the Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) [9] was how difficult the task is from the animal health perspective. The fact that you have different species and communities that you have to treat and sustain health for economic and political reasons is a huge burden on countries especially the Middle and Low Income Countries (MLIC).

Dr. Balkhy: The next question is to Dr. Albatshan, as the deputy Minister for the Ministry of Environment, Water, and Agriculture (MEWA) in the Kingdom of Saudi Arabia. Your role crosses between animal, plants and water, all of which have an impact and or role in the emergence of AMR. During the recent Joint External Evaluation (JEE) [12] your team was heavily involved in the aspects relevant to this topic as were many of the GCC and Middle East and North Africa (MENA) countries. My question is, what are the challenges in controlling antibiotic use in animal health in Saudi Arabia?

Dr. Albatshan: Thank you Dr. Balkhy for engaging me in this important discussion. AMR is now among the top priorities of our ministry here in the Kingdom of Saudi Arabia. We need to understand what is actually happening to better educate our veterinarians on this important topic. The following are the three routes through which antibiotics reach animals. Firstly, through feeding: to promote the growth of animals for economic purposes. Secondly, through water: used as medication to treat communities, mainly in the poultry sector. Unfortunately, this route is abused the most because it is being used as a precautionary practice and not as treatment. And finally, through direct injection: used mainly in livestock as a treatment method.

Antibiotics can be added through the feeds in the feed mills to be consumed by animals. As growth promoters, fortunately it was banned from the country 15 years ago. Feed manufacturers are not allowed to add any antibiotics through the feeds whether for treatment or for growth promotion. This is quite regulated and monitored by the Saudi Food and Drug Authority (SFDA). Several steps have been implemented in the past to ensure that antibiotics are not being used for this purpose.

The second route is through the use of antibiotics to treat communities such as in poultry houses with about 30,000 birds and since we cannot treat one bird at a time, we must treat all the birds at the same time. Sometimes there is a high rate of abuse in this area because it is used as a preventive measure and not as treatment. If we visit poultry houses in Saudi Arabia, we can see the usage of antibiotics in the administration of water as a precautionary measure for the malpractices that happen in this field. The third route, which is also under control of the MEWA, is the counter prescription of antibiotics for the traditional sector in livestock, such as sheep, camels, lamb, etc. Only recently, we have started monitoring this sector. It is ensured that the administration of antibiotic through the feed is regulated and there is no abuse in this area in which we are not aware of. But most of the time, we find the abuse of antibiotic in the water in the egg laying farms, poultry and meat industry. MEWA continuously monitors these sectors and cites such breaches in practices. Examples of such citations are posted on the MEWAs twitter account, in a way of announcing such infractions to the public. Fines on such practices may reach half a million Saudi Riyals; which is close to 130 K US dollars or closing down the farm. The implementation has been active for the past 10 years and we find some abuses from time to time for which we have taken strong measures. In general, it is a goal for all of us whether physicians or veterinarians and we know that it is hard to control the use of antibiotics if no penalties are in place.

Dr. Balkhy: Thank you Dr. Albatshan, this is very valuable information. You have highlighted very important disciplinary measures needed to control the misuse of antibiotics in animals. May you please highlight the challenge of controlling these agents in what is known as backyard farming in Saudi Arabia.

Dr. Albatshan: Yes, indeed animal care falls under two sectors: the first is the organized industrial sector where we have excellent control over their feeds, medication, and conduct regular surveillance. And the second is the traditional farming sector, or what you referred to as backyard farming. The traditional sector is a big challenge. I am referring here to the sheep, camel, and cows with traditional farming where we are struggling the most. All farms have access to antibiotics and may administer these antibiotics in any form; even in the water if they wish to do so. We do not have much control over these practices. However, we are working with our colleagues in the Ministry of Municipalities to go to slaughterhouses that will be monitored properly in the future. If the animals are sold directly in the market we may not have much control over them, but if the animals first go through the processing plant, then that can be regulated and monitored by the Ministry of Municipalities and there have been steps taken to ensure supervision and regulation to limit or hopefully to eliminate the spread of AMR from this route.

Dr. Balkhy: Thank you Dr. Albatshan. The next question is to Dr. Aidara-Kane, there have been major efforts to identify the critical antimicrobials needed for human health in order to limit their use in the animal sector [10]. So, is there evidence that the rise in antimicrobial resistance in pathogens infecting humans originates from the misuse of antibiotics in animals? I know this is a tricky question, and I would also, like to ask you to highlight to the audience, please, the efforts of the AGISAR Committee on providing guidance on Critically Important Antibiotics (CIA) that we as human health providers assume they should be never be used in animals, while the animal health providers find that they should still be used to preserve animal health?

Dr. Aidara-Kane: Developing the CIA list was a request from the tripartite (WHO-FAO-OIE) during a tripartite expert meeting held in 2004 [13]. It was not the WHO that decided to do this but it is an outcome of the tripartite meeting, which assessed the risks of
antimicrobial resistance from the food chain to humans. Considering that antimicrobials used in the animal sector are more or less the same as those used in the human sector, WHO and OIE were requested to collaborate with the animal sector on which agents are critical for human health and thus should be avoided in animals as much as possible. The overall objective is to protect and preserve the effectiveness of antibiotics that are most critical for human health [14]. WHO developed the list in 2005, and we update this list every two years taking into account the emerging resistance threat and new antimicrobial drugs that become available on the market. In the current version [10] we now have five classes of antimicrobials that are the most critical ones: quinolones, 3rd, 4th and 5th generation cephalosporins, glycopeptides and very recently Polymixin (colistin) was added. On the human side, we have made great efforts to impose stricter rules on availability of these drugs. Good practice tells us that an antimicrobial susceptibility test should be done and that will assist in prioritizing the use of the narrow spectrum antimicrobials instead of starting directly from the broad spectrum ones such as quinolones.

Our expectation from the animal side is that they should also make efforts to preserve these antimicrobials. For the most critical drugs on the WHO CIA list that are also on the OIE list of Antimicrobial Agents of Veterinary Importance, OIE advises that these should not be used for treatment unless based on the antimicrobial susceptibility testing, and should never be used for growth promotion. We have antimicrobials on our list that are not on the OIE list and our recommendation is that we do not want them to be used as growth promoters as everyone agreed and we would like to see them protected. WHO has also been working on recommendations on how to use the WHO CIA list to guide optimal antimicrobial use in food producing animals, using very strict WHO guidelines and development procedures for the development of evidence-based recommendations. For this purpose, we have commissioned systematic and literature reviews to inform a committee that is working on assessing the evidence and formulating the recommendations as a formal WHO Guidelines based on the WHO CIA list. This work is in progress, and while I cannot share the outcome of the recommendations for the moment, I can assure you that they will be of interest to this group and globally to move the AMR agenda forward.

Dr. Balkhy: Thank you very much Dr. Aidara-Kane. My next question is directed to Dr. Alhawaswi, Director General, Saudi Patient Safety Center (SPSC). From the clinical practice point of view, we notice the misuse of antibiotics at all levels, which has contributed to the rise in AMR. What is the role of the SPSC in the Kingdom of Saudi Arabia in combating the emergence of AMR?

Dr. Alhawaswi: Thank you Dr. Balkhy for inviting me to be part of this landmark activity. The SPSC has been in existence for two weeks only, but the national efforts for improving patient safety goes back for many years. I was fortunate to be with the Saudi Central Board for Accreditation of Healthcare Institutions (CBAHIs) for quite a while now, and as you said this is a major patient safety initiative. However, the accreditation as an isolated activity will not have the needed impact in improving patient safety. The SPSC complements the four existing major components of the Saudi Healthcare system today, namely:

4) The Council of Cooperative Health Insurance, that regulates health insurance in the private sector.

There is a major initiative for transforming the whole healthcare system with in Saudi Arabia and we understand the need for creating collaborative efforts between the different components of regulators in order to improve patient safety as part of this transformation. So discussions on how to coordinate efforts among all four entities to improve patient safety have been taking place. On matters of AMR and the misuse of antibiotics, SPSC is aiming to coordinate between the SMOH and the SFDA to abandon over-the-counter (OTC) dispensing of antimicrobial agents over a grace period of time to ensure public safety as its first and most critical mandate.

I would like to take a minute to refer to a recently published paper, which looked at self-medication with antibiotics in the Middle East [15]. It ranged anywhere from 19 to 80%. The three main sources for access to the antibiotics cited in this paper were:

1) Pharmacy dispensing OTC medication without prescription.
2) Sharing medications at home through parents and elders who store and save them in the fridge.
3) Sharing medications among friends.

These situations need to be addressed through public awareness campaigns. It may be hard to regulate from home but on the community level, especially among pharmacists, a lot of improvement may be done. At the community level, close coordination among the four different regulators, as I had mentioned, would complement the work of any antimicrobial stewardship program based in hospitals.

Dr. Balkhy: You are giving us a good point and your comments and interaction with the earlier presentations are useful. I remember during our basic training as physicians, we needed to be educated on how to educate patients going home with antibiotics upon discharge. One of the teaching points is not to share your medications with anyone else. However, some countries go a further step and offer incentives to those who return remaining antibiotics back to the hospital or pharmacy. I do not know if we will ever reach that level but if we have all the right tools in place we may be able to do so.

Dr. Balkhy: The other big element that we have not been discussing is the impact of environmental contamination on AMR; whether from pharmaceutical waste or animal waste or waste from the healthcare facilities. Hopefully we will in future meetings. But as a follow up question to you Dr Alhawaswi; what are your thoughts on the excess of antibiotics from human use, where does it go, and how can it be managed?

Dr. Alhawaswi: I had a recent conversation with the SFDA and they are working on an interesting initiative called the “track and trace” [16]. They refer to Turkey as the only country on the planet that has full track and trace practices. You basically track the medication from the time it was manufactured till it reaches the end users. We hope this will be the classic form for our patient safety initiatives. Added to this area are a lot of fraudulent behaviors between the insurance companies and the community pharmacies where this track and trace initiative may be overridden. It is not only the individual that gets harmed with such behaviors, but actually it creates more AMR that burdens the whole community.

Dr. Balkhy: Thank you Dr. Alhawaswi and I wish you all the best in running this new entity in Saudi Arabia and we will be watching the progress very closely. My next question is for Dr. Albatshan: what is the role of MEWA in limiting the spread of AMR through the environment; has this been looked in to?

Dr. Albatshan: In relation to the environment, there is a new mandate at MEWA. Generally, the environment has been a major

1) The Saudi Commission for Healthcare Specialty that certifies healthcare professionals in Saudi Arabia;
2) The Accreditation of Healthcare Institutions (CBAHII) that accredits healthcare facilities in Saudi Arabia;
3) The Saudi Ministry of Health (SMOH), where a new Deputy Chief for Compliance provides licensure for healthcare systems, recently approved and appointed, and;
concern and we have been talking about it for some time now. Also, a scientist informed us recently of findings on highly resistant microbes in the sewage system of the city of Jeddah. My colleagues have been warned about this issue and we are developing a strategy for the control of the release of waste highly contaminated with antimicrobial agents into the environment. We will need to look into the risk posed by pharmaceutical companies, of which we do not have many by the way, and whether they have clear control over their waste. The SFDA is the authority that licenses such companies, allows importation, and knows exactly what is happening in the country with medication; so we will be working hand in hand with the SFDA on this issue. Further, we are trying to create an electronic link with the SFDA to know what type of medications are being imported or manufactures in the country and used by the industries. Our ministry also has a huge initiative to develop an electronic platform for all veterinary clinics, which will include the veterinarian pharmacies that are operational in the Kingdom. This way we will be able to track all dispensed medications, and their indications by any veterinarian in the Kingdom. With the SFDA launching the “track and trace” initiative mentioned by Dr. Alhawsawi, the Kingdom of Saudi Arabia will enter a new era. I hope we will be able to update you on our progress during the next meeting.

Dr. Balkhy: Thank you Dr. Albatshan. I would like to ask you if there are any other specific initiatives to enhance the role of auditing at MEWA and what is the vision to enhance the role of risk assessment in your ministry.

Dr. Albatshan: Indeed, I would like to add to my colleagues in the veterinary sector that we have just started to add a new department at MEWA focusing on internal inspection on health and veterinary practices. Previously, we only had one department called “Animal Resources” dealing with these issues. But this was found to not be sufficient and the mandate was too wide and needed certain expertise. With the new structure, there are now two departments: one is concerned with the health inspection of all the veterinary sectors, drafting strategies and working with our colleagues in the SMOH, SFDA on major issues of AMR. The other department is focused on Risk Assessment of these issues.

Conclusion and recommendations

Dr. Balkhy: I would like to thank the participants for a great discussion, but before we end may I ask each one of the panel members for two to three recommendations that would help the stakeholders in controlling AMR at the national and regional levels?

Dr. Alhawsawi: My main recommendation falls under the word collaboration. We need to benefit from all the expertise that exists in the country under the different sectors and work together for our single goal. This goal is to improve human health. This, by the way, is aligned with the current healthcare transformation initiatives taking place in Saudi Arabia today; where the set goal is to improve life expectancy from 74 to 80 by 2030.

Dr. Albatshan: Words of wisdom, AMR is not an easy topic to address nor does it fall under a single area of concern. So not only do we need to address the veterinary sector but also all sectors need to move forward together. You are keeping an eye on our practices, and we are also keeping an eye on your practices in the human health sector. We are going to work as a team. Physicians have the burden of finding evidence as they investigate veterinary practices, while veterinarians are also concerned with the human medical practices. Hence, working as a team is necessary.

Dr. Aidara-Kane: I am delighted with the strong commitment that we see today at the highest levels of many organizations around the world. At the global level, we have commitment from the Heads of States, the WHO, ministries of health. Opportunities must be seized to tackle this as an important issue. It is a shared responsibility, and it is not about pointing fingers at one another. Each and every sector has to do their share of what needs to be done. Most importantly, there is real need to work together on integrated surveillance. There is a need to share data and information from the human and animal sectors, and from the environment to tackle this issue from a “One Health” perspective. As a global community we need a lot of momentum and action from local communities among the different sectors at the national level.

Dr. Erlacher-Vindel: I am very impressed with the progress that has taken place in the Kingdom of Saudi Arabia from the agricultural side; it is very encouraging. The actions should be aligned to global standards and translated in the local environment of each country. And that is what I sensed today. Secondly, we need to find ways to come up with a common understanding on AMR from all sectors and this may take a while. I emphasize this because it is easy to preach; however, implementation is another level. So identifying and understanding the local circumstances is important for proper implementation. Finally, participation in the global surveillance monitoring system should be highly encouraged because it reflects the global engagement of the regions and sub-regions and individual capacities.

Dr. Balkhy: I would like to thank all the speakers for their great insight and information and to the audience for being with us during this session. We will have a short break and be back in the afternoon for the second roundtable discussion that will focus on human health.

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References


