The AfSPID BULLETIN

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CONTENTS

EDITOR'S COMMENTARY

Dear Colleagues

Welcome to the tenth edition of our newsletter.

At the 11th World Society for Pediatric Infectious Diseases congress in The Philippines in November 2019 Dr Paula Vaz gave a fascinating talk on the impact of cyclones Idai and Kenneth in Mozambique. She has kindly converted her talk into a commentary on the infectious disease risks posed by these natural disasters and the Mozambican response to mitigate these risks. This commentary is featured in this edition of the newsletter.

Since SARS-CoV-2 emerged in Wuhan, China in December 2019, it has spread with alacrity causing millions of infections, hundreds of thousands of deaths, and massive social disruption and economic devastation. Although the direct impact of coronavirus disease 2019 (COVID-19) has been substantially lower in children than adults, mathematical modelling predicts that the indirect impacts of the pandemic, including disruption to routine health care and reduced access to food may result in large increases in maternal and child mortality in low- and middle-income countries. Furthermore, the emergence of multisystem inflammatory syndrome in children (MIS-C) temporally related to SARS-CoV-2 infection has stimulated interest in the interaction between SARS-CoV-2 and the immune systems of children and adolescents. The COVID-19 pandemic is indeed dominating the thinking and practice of academics and clinicians throughout the world including Africa. This is reflected in the spectrum of papers published in this edition of the newsletter. We feature four articles on COVID-19 written by authors working in three African sub-regions, a commentary on BCG vaccine by Professors Hussey and Hatherill, both world authorities on tuberculosis vaccines, a short report on the challenges of identifying paediatric COVID-19 in Africa by Dr Alemayeshu, an in depth review of COVID-19 by Dr Ogunbosi and Professor Oladokun in which many thought provoking questions about COVID-19 are highlighted towards the end of their paper, and finally an overview of the negative impact of the COVID-19 pandemic on childhood immunisation programmes by Professor Nte.

Leishmaniasis, an ancient protozoal disease is also featured in this newsletter. It has affected human populations in Africa for several thousands of years. The earliest evidence of human *Leishmaniasis donovani* infection was obtained in Egyptian and Nubian mummies dating back to 3500 to 2800 years before the common era. Furthermore, DNA evidence suggests that Sudan may have been the original focus of visceral leishmaniasis [refer Emerging Infectious Diseases 2006;12(10):1616-17]. Today, leishmaniasis is found in 89 countries but is highly endemic in East Africa and the Indian subcontinent. The World Health Organization recognises leishmaniasis as one of 20 neglected tropical diseases, a diverse group of tropical infections which are common in low-income populations in poor regions of Africa, Asia and the Americas and caused by a variety of pathogens such as viruses, bacteria, protozoa and parasitic worms (helminths). In this edition of the newsletter Dr Mulugeta Naizgi Gebremicael discusses diagnostic and treatment challenges of visceral leishmaniasis in Ethiopia in a well written paper.

In February 2020 I co-convened our department's annual paediatric refresher course. The Department of Paediatrics and Child Health, University of Cape Town and Red Cross War Memorial Children's Hospital have convened annual refresher courses since 1974. The 2020 course, featured rheumatology, immunology and infectious diseases and was preceded by two day-long workshops, one on rheumatology attended by 27 delegates and the other on the primary immune deficiencies attended by 48 delegates. The 3-day course was attended by approximately 300 paediatricians, medical officers and nursing personnel. In addition, it was live streamed to one of the lecture theatres at Red Cross War Memorial Children's Hospital so that clinical staff members who had to continue working at the hospital could attend. The primary immune deficiencies workshop featured South African experts who addressed various aspects of the discipline including clinical presentation, immunological diagnosis genetic diagnosis immunoglobulin replacement

therapy, haematopoietic stem cell transplantation, autoinflammatory conditions, immunization practice and antimicrobial prophylaxis, refer Figure 1.

Figure 1: Participants at the recent workshop of primary immune deficiencies.

The refresher course proper featured a wide range of infectious diseases topics including advances in treating bacterial infection, β-Lactam / β-lactamase inhibitor combinations for invasive Gram-negative infections, Clostridium difficile infection, congenital CMV infection, Malaria, drug-resistant tuberculosis influenza, antiretroviral advances and childhood immunisation. Furthermore, two of three plenary presentations featured international speakers namely, Professor Michael Levin of Imperial College on differentiating viral and bacterial infections and Professor Adilia Waris from the University of Aberdeen on invasive fungal infections. Whether or not the next paediatric refresher course scheduled for February 2021 will be conducted conventionally in a conference hall or because of the COVID-19 pandemic hosted through a digital platform has yet to be decided, refer Figure 2.

Figure 2: Dr Elizabeth Goddard presenting her talk on immunoglobulin replacement therapy at the recent workshop of primary immune deficiencies

Although, overshadowed by the COVID-19 pandemic Ebola remains a persistent challenge on the African continent. The 10th Ebola outbreak in the Democratic Republic of Congo (DRC) in the eastern provinces of North Kivu and Ituri was declared on 1 August 2018. Despite extensive use of a ring immunisation strategy to contain this outbreak, it has run a protracted course because the public health response was undermined by chronic conflict and insecurity in the area of the outbreak as well as by direct, violent attacks of health care workers involved in the outbreak response. Fortunately, this outbreak appears to be coming to an end. No new confirmed cases have been reported since 27 April 2020. As at 11 June 2020 the outbreak has caused a total of 3463 Ebola virus disease cases, including 3317 confirmed and 146 probable cases, of which 2280 cases have died, an overall case fatality ratio of 66%. Unfortunately, on 1 June 2020 the World Health Organization was informed that a new Ebola outbreak was declared in Équateur Province in DRC. As at 8 June 2020, this new outbreak has caused 12 Ebola virus disease cases, of whom 8 were fatal.

Development of the programme for the 12th WSPID conference has commenced. Within the next few weeks the International Scientific Committee will have its first conference call to formally discuss the organisation of this conference. It is scheduled to take place in Mexico in 2021.

I'm very pleased with the spectrum of interesting topics addressed in this edition of the newsletter. I hope that you also enjoy its contents.

Kind regards, Brian Eley

INFECTION RISK IN THE AFTERMATH OF CYCLONES IN MOZAMBIQUE

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INTRODUCTION

On 14 March 2019 Cyclone Idai made landfall in Beira affecting 3 million people and killing more than 700 people in Mozambique, Malawi and Zimbabwe. Six weeks later on 25 April 2019 Cyclone Kenneth hit Cabo Delgado, affecting another million people. There is no country record of such a humongous disaster! Massive destruction of houses (100,000), roads, bridges, communication networks, and water and power supplies left people in total despair.

Figure 1: Photograph by Andre Catueira / Keystone (https://www.caritas.ch/en/what-we-do/worldwide/disaster-aid/aid-for-the-victims-of-cyclone-idai-in-mozambique.html)

This situation favoured the emergence of outbreaks and other health issues that needed to be immediately addressed to control further damage. Several factors contributed to an increased risk of infection such as displacement of people into overcrowded camps, cross-contamination of water sources, proliferation of mosquitoes increasing the risk of a surge in malaria incidence, unplanned and overcrowded shelters, poor water and sanitation conditions, poor nutritional status and insufficient personal hygiene, in addition to disrupted health services.

Infection risk control in the post-cyclone period is generally considered in 3 different phases (Kouadio Koffi Isidore, 2012): Phase I or the impact phase usually lasts 0-4 days. In this phase actions are directed towards initial treatment of disaster-related injuries. Phase II or the post-impact phase lasts 4 days to 4 weeks. During this phase the first waves of infectious diseases (air-borne, food-borne, and/or water-borne infections) might emerge. Finally, Phase III or the recovery phase occurs lasting for more than 4 weeks. During this last phase, infections with long incubation periods or latent-type infections occur, and infectious diseases that are already endemic and infections newly imported into the affected communities, may spread and become epidemics.

In parallel, Mozambique has a high prevalence of HIV and tuberculosis and patients infected with these diseases should continue on treatment without interruption. Therefore, the systems in place to prevent outbreaks, should accommodate chronic patients and their health needs.

Providentially, a broad humanitarian response which includes governments, international agencies, local partners, the private sector, groups and individuals was quickly mobilized to provide an efficient response.

RESPONSE

The cyclones demanded a comprehensive and integrated emergency response, described to the different phases i.e. phases I, II and III and the respective key activities undertaken in each phase.

Phase I: Immediate response

This started on day one and lasted over six months. National authorities and partners acted quickly to respond to the emergency under the leadership of the National Institute for Disaster Management (INGC). With the objective of reducing preventable mortality and morbidity through the provision of essential life-saving health services, the Ministry of Health (MoH) activated its Public Health Emergency Operational Centre, led by the Minister of Health and Rapid Response Teams at national and provincial levels. The Country Humanitarian Team activated nine groups to support the government-led response, namely Education, Food Security and Livelihoods, Health, Water and Sanitation, Emergency Communication, Nutrition, Protection, Shelter (accommodation centres) and Logistics.

In parallel with community rescue activities, transient accommodation centres were established at closed schools with health service posts, providing medical, psychological support and / or appropriate referrals as required. Intense work begun to re-establish communications, air transportation and health and sanitation services.

Coordination of the Multiple Response of Partners at National and Provincial Level

National and Provincial Emergency Centres (PECs) were established for planning and coordination, and monitoring of all field activities, ensuring coordination with health partners and between health and nutrition groups. PECs organized and coordinated needs assessments comprehensively, including risk assessments for the affected population by health professionals and local leaders. Furthermore, PECs analysed the risks posed by the context and environment, both in community settlements and urban areas. In addition, PECs coordinated the flow of people to the accommodation centres. Timely information on results, including maps, was provided every week. Daily meetings and updated daily and then weekly bulletins ensured strong communication and information was distributed to all involved in the response.

Phase II: Post-impact phase

During Phase II that started more than a week after the cyclones struck. The infection control response was based on four pillars: re-establishment of health services, community and environmental health, chronic infectious diseases and prevention and control of outbreaks.

Restoring the functionality of primary and secondary level health services

To restart the health system, we had to configure primary health care services based on the available resources. This was done through health facilities that were not damaged, sending mobile brigades to health posts that had been established at accommodation centres, using mobile brigades or community agents (APEs) to service remote and isolated communities. Furthermore, health professionals including regional and international medical teams were repositioned to address new priorities and ensure uninterrupted essential and priority services i.e. sexual and reproductive health, mother-and-child health, immunization, vitamin A supplementation, triage, malaria prevention, TB, HIV & AIDS and health promotion. A special task force for psychosocial support and gender-based violence was put in place a few weeks later to manage emerging violence issues and post-traumatic stress among other mental health issues. Referrals and counter-referrals within the health system were also re-designed as well as health and sanitation services for the displaced population at transitory and permanent locations.

HIV infection in emergencies: Humanitarian standards established a minimum initial service package with activities aimed at reducing reproductive health morbidity and mortality in emergencies, which includes the availability of free condoms, prevention and management of sexual violence and comprehensive reproductive health services, including attention to the situation of adolescents living with HIV. To implement this package, the activities focused on population sensitization regarding the risks of contracting STIs and HIV infection and preventive measures, communication about gender-based violence both in households and public spaces, access to condoms and counselling, and treatment, especially antiretroviral treatment (ART). Since patients on ART are registered in an electronic database at the health facilities, the tracking of these patients at shelters was done to prevent treatment interruptions. For **tuberculosis,** medicines were supplied and patients tracked at the temporary accommodation centres. In addition, active case finding was implemented for patients missing at the health

facilities. Testing and screening were available at the shelters.

Community health activities done by community agents: APEs affected by cyclone Kenneth were identified and based on a survey of the situation of the APE Work Kit (Medicines, Bicycles, Vests, Stopwatches, Boots, Raincoats and Briefcases), the Medicine Kit and working materials were replaced. The APEs were integrated into community work groups while a census of affected families and mapping of resettlement areas allowed for their repositioning, so that they could carry out routine activities in relation to newborn care, diagnosis and treatment of malaria, distribution of supplements (vitamin A), condoms, water purifiers and door-to-door promotion and prevention activities such as hand washing messages and the construction of latrines.

Environmental health: Key activities included quality control of water for human consumption, checking the hygienic and sanitary conditions of temporary accommodation centres and communities, ensuring that water tanks were cleaned and disinfected, and dissemination of key messages for preventing water-borne diseases through mobile radios. Furthermore, information and education about individual and collective hygiene, food hygiene, water treatment at home, correct use of latrines and proper management of solid waste were discussed using community radios and disseminated through community agents.

Support for the referral network: In a context of many access limitations, it was crucial to implement a referral system from the peripheral level to the district headquarters and from the district to the province.

Prevention of and Response to Infectious Diseases Outbreaks: Prevention of outbreaks focused on improving access to clean water and sanitation and the establishment of a surveillance centre with sentinel sites. INS was able to quickly set up surveillance systems for diarrhoeal and respiratory diseases and malaria, considering that both cholera and malaria are endemic in the regions affected by the cyclones.

Acute diarrhoea, dysentery and cholera: The mechanism for early warning was strengthened and closely monitored so that health authorities were informed of cases and thus could generate alerts for immediate response. INS established outbreak investigation teams to ensure that (1) a response was triggered quickly when an alert was generated, (2) samples were tested by rapid diagnostic tests or laboratories to confirm an outbreak, and (3) an appropriate response was achieved. We were prepared to prevent outbreaks of diarrhoea, dysentery, cholera and measles. The team conducted daily and weekly surveillance of diarrheal diseases. The rapid response teams for cholera quickly acted to identify cases and refer them for treatment at cholera centres established in strategic urban neighbourhoods, while delivering water, sanitation and hygiene (WASH) messages, cholera kits and education and toilet disinfectants, and monitoring water for residual chlorine. By the second week after the cyclones struck, an outbreak of cholera was declared despite all efforts to improve water and sanitation. A cholera immunization campaign commenced four weeks after the cyclones struck, in the more densely populated areas. Two rounds of immunization were administered one month apart.

Malaria: Malaria was the primary cause of morbidity and mortality both in adults and children. Actions taken to prevent malaria and ensure early diagnosis and timely treatment, included the distribution of mosquito nets to all affected families and anti-malarial drugs to primary health care and accommodation centres.

Phase III: Recovery phase

During this last phase, infections with long incubation periods or latent-type infections may occur, and infectious diseases that are already endemic and infections newly imported into the affected communities may spread and become epidemics. In addition, preventing malnutrition is important as it increases the risk of infection. Active surveillance continued for water, and airborne diseases and malaria.

Provision of immediate nutritional support for children under five years and pregnant and lactating women

A nutrition cluster was created by the nutrition department of the MoH to support the coordination, supervision and monitoring of the nutritional response in the affected areas.

This cluster organized active screening of displaced populations in the affected districts to identify cases of malnutrition. This was done by mobile brigades to ensure the nutritional rehabilitation of affected individuals. The stock of supplements, therapeutic products, food and nutritional supplements received a boost from international donors. The response to these interventions was guided by nutritional monitoring and surveillance. Provision of essential micronutrients and vitamin A, deworming, and immunization for children between 6 and 59 months was executed in campaigns at functional health facilities and the shelters.

Logistics, monitoring & evaluation

Establish logistics and operations support: Strong logistical support was at the core of the response. The main infrastructural, procedures and operational support must exist to enable all aspects of the health sector's response. Mapping the interventions, coordination of logistical capacities, effective management systems to ensure the availability and safety of essential medicines and medical equipment, including transport, storage and cold chain management of vaccines were undertaken by a specific cluster coordinated by the United Nations Office for the Coordination of Humanitarian Affairs (OCHA), who worked closely with the MoH and international agencies to ensure the provision of logistical, communication, subsistence, transportation and fuel support for the rapid response and surveillance teams.

Monitoring, Reporting and Evaluation: It is crucially important that all partners involved in the response are kept up to date with accurate information to ensure that the response was highly effective. Thus, the objective of health information management and reporting was to ensure that all health respondents received the latest information on the population's health and nutritional status and outbreak threats, the availability of health services and use of health services, and identification of patients with chronic diseases and their re-integration into appropriate services. Therefore, minutes of daily meetings, weekly epidemiological updates and periodic reports of key health and nutrition indicators were shared with all health respondents.

RESULTS

The first 3 months

Results included the assessment of the impact of the afore mentioned strategies on acute diarrhoeal disease notification, cholera, malaria and acute respiratory diseases, in parallel with patients with chronic diseases lost to follow-up, especially HIV-infected patients. A cholera outbreak was declared and controlled. There were no other outbreaks or expansion of cases of existing infectious diseases.

A total of 1 million people received the oral cholera vaccine; 800 000 in Sofala and 200 000 in Cabo Delgado; both regions had been affected by Idai and Kenneth. The number of daily cases for cholera declined progressively during May 2019, as shown in Figure 2

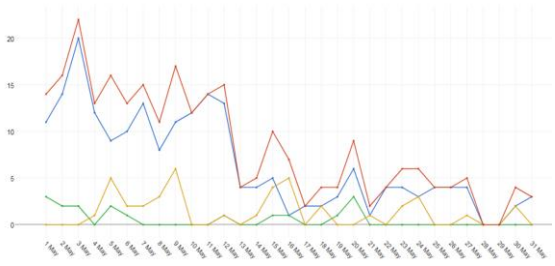

Figure 2: Cholera cases declined progressively throughout May 2019, 4 districts, Cabo Delgado, a Cyclone Kenneth affected area

Source: INS, SITREP Bull 9, 2019

After 6 months

In the Idai affected districts there remains 68 active resettlements hosting more than 80 thousand people while in Kenneth affected districts there are 2 active resettlements. (MoH, 2019) Basic health service provision remains a challenge among the displaced population and the government with health partners are working to renovate the damaged health facilities and improve access to basic health services through mobile brigades.

Malnutrition reports indicate that there are 2.1% cases of acute malnutrition which is under existing malnutrition rates in the affected regions. (MoH, 2019) An unusual increase of pellagra cases occurred in one district affected by cyclone Idai requiring a bigger supply of nicotinamide than existed, resulting in stock-outs. This problem is being closely monitored.

There have been no cholera cases registered in any of the districts for more than 3 months. (MoH, 2019)

After reaching a peak in May 2019, the number of malaria cases declined as shown in Figure 3, (MoH, 2019) however, cases reported in the sentinel sites remained in the average range reported in previous years (INS, 2019).

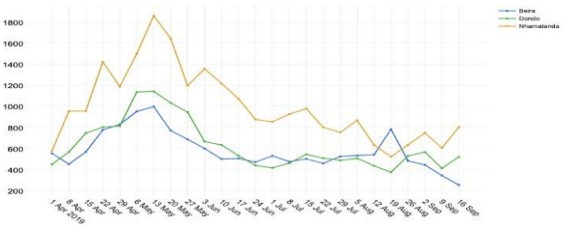

Figure 3: Malaria cases declined between April and September 2019 in sentinel sites in 3 districts of Sofala

Source: sitrep, bulletin 11. INS, WHO, MoH.

By December 2019, according to UNICEF a total of 812,065 people were reached with safe water, 124,028 people benefitted from sanitation and hygiene promotion activities including point-of-use water treatment safe practices, 673,614 children under 15 were vaccinated with oral cholera vaccine and/or measles vaccine, 31,541 children received psychosocial support through safe spaces, 1,525,376 people were reached with key lifesaving and behaviour change messages, 363,934 people accessed appropriate sanitation facilities and received hygiene messages, 8,346 pregnant women aged 15-49 and living with HIV received ART and 456,726 children aged 6-59 months received routine vitamin A supplementation. (UNICEF, 2019)

CHALLENGES

There were and still are many challenges relating to health services provision, infrastructure, human resources and disease control. Difficulties prior to the cyclones are even more significant. Airborne diseases and TB control were not as well surveyed as water-borne and food-borne diseases and better strategies are needed.

Data availability and reporting from health facilities face challenges due to high rotation of health professionals and work overload of the existing professionals leaving little time for monitoring and data quality activities although these activities are not less important that direct clinical activities. Nevertheless, INS is working closely with the provincial MoH structures to strengthen reporting.

WHO is closely working with INS and the MoH, supporting EWARS reporting efforts through information sharing and provision of training for health professionals and data technicians.

CONCLUSIONS

The cyclones hit hard and caused huge devastation. It will take decades to recover the infrastructure and heal the psychosocial scars.

Amidst the needs and priorities, key lessons learned are worth mentioning. Strong planning and coordination with open communication are the most important elements of a successful response. A rapid and well-coordinated comprehensive response is critical to control risk infection. In parallel, re-establishing and improving the delivery of primary and secondary health care is vital.

Practically, prompt and adequate prevention control measures, appropriate case management and surveillance systems are vital for minimising infectious disease risk. Furthermore, education on hygiene and hand washing, and the provision of safe water, sanitation facilities and shelter for preventing infectious diseases are essential elements of an effective response. Infrastructure renovation may take a long time but shouldn't prevent health service delivery from getting back on track.

In the aftermath of the cyclone, a comprehensive needs assessment followed by a coordinated WASH strategy, cholera immunization programme and mass information and education campaigns are at the core of diarrheal disease prevention and cholera control. Interventions included supporting oral cholera vaccination, establishing well-functioning cholera treatment centers, epidemiological

surveillance, upgrading the cholera treatment unit, staffing, and water and sanitation activities. The outbreak was quickly brought under control. Surveillance efforts continue for priority diseases such as diarrhoea and malaria.

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BCG AND COVID-19: IMPLICATIONS FOR SOUTH AFRICA

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The anecdotal evidence for a positive impact of Bacille Calmette Guerin (BCG) vaccine on COVID-19 disease comes from an ecological study in which morbidity and mortality rates from COVID-19 in various countries are compared in relation to their use of BCG vaccine in the past (Miller et al, medRxiv preprint doi: https://doi.org/10.1101/2020.03.24.20042937; not peer reviewed). The authors suggest that countries with well-established BCG vaccination programmes have better outcomes compared to countries without such programmes.

What are the implications for South Africa?

BCG vaccine was first used in 1921 to prevent tuberculosis. The original BCG vaccine was not cloned but was distributed to a number of laboratories worldwide. This has resulted in a number of related BCG vaccines with varying phenotypic and genomic characteristics – the point is that not all BCG vaccines are the same. The five main strains used in the last 2-3 decades, accounting for more than 90% of the world's production, are the Tokyo, Russian, Danish, Pasteur and Moreau strains. These strains also induce varying immunological responses and potentially also variable protective efficacy against pulmonary TB. The estimates from clinical trials range from 0-80% with an average protection rate of only 50%. BCG does, however, protect against the more severe forms of TB in infancy, including miliary TB and tuberculous meningitis. Meta-analyses of published studies report that protection is of the order of at least 80%. BCG vaccine also protects against leprosy and provides some protection against Buruli ulcer caused by *M. ulcerans*.

Somewhat controversial evidence suggests that newborn BCG vaccination may improve overall infant survival, independent of protection against TB, through "heterologous" or nonspecific protection against respiratory infections in early infancy, by the mechanism of "trained immunity" (Moorlag et al, Clinical Microbiology and Infection 2019). This hypothesis is suggested by Miller et al as a possible reason why BCG vaccination might protect against COVID-19.

In South Africa, BCG has been used sporadically since the early fifties and was first administered to school-going children. However, from 1973 BCG has been given universally to all newborn infants with very high coverage. Therefore, South African adults aged 45 years old or younger probably received BCG vaccine (these will include large numbers of our health work force) and those between 45 - 65 years possibly received BCG, but it is unlikely that those older than 65 years of age received BCG vaccine. Given that the non-specific beneficial effects of newborn BCG vaccination are thought to be short-lived and limited to early infancy, it seems unlikely that programmatic BCG vaccination of South African infants might confer long-term protection against COVID-19 mortality that mainly affects the elderly.

A related question is whether older South African adults, who may not have received BCG vaccination in infancy or childhood, should be vaccinated with BCG to possibly prevent or mitigate the severity of COVID-19 infections as suggested by Miller et al.

The first point to note is that ecological studies such as the one by Miller et al do not prove causality and we have to be mindful of the potential for over-interpretation of results and generation of potentially spurious findings from such studies. There are also problems in how the authors interpret the data. For example, other important factors that might lead to major differences in COVID-19 infection and mortality rates in countries with high vs low BCG vaccination coverage, such as socio-demographic factors, season, climate, COVID-19 testing rate, and the relative "maturity" of the country-level COVID-19 epidemic, are not evaluated as potential confounders.

It should be noted that there are no data to confirm whether BCG vaccine is safe in older adults. Using any vaccine in elderly needs to be studied to ensure that it is safe and does not cause problems. BCG vaccine is a live attenuated vaccine and should definitely not be administered to individuals who are immunocompromised as it can lead to significant complications. The ageing process is also associated with a decline in immune functioning in general (called immunosenescence and thus there may be issues with using a vaccine like BCG in this age group.

It is also likely that >80% of older South African adults will have been exposed and asymptomatically infected with "latent" TB during their lifetime. Since TB is a mycobacterium very similar to BCG vaccine, and latently infected people show similarities in immune response to BCG-vaccinated people, it seems unlikely that BCG vaccination of older adults would offer additional non-specific protection against COVID-19. It is conceivable that BCG revaccination of adolescents and young adults without latent TB infection might offer some non-specific benefit against COVID-19. This hypothesis can be tested retrospectively in an ongoing South African trial (BCG REVAX), which is currently paused to recruitment due to the COVID-19 lockdown.

BCG vaccine administered to an individual who has been previously infected with tuberculosis may result in a significant adverse reaction at the site of vaccination. This is important in the SA context where exposure to tuberculosis is virtually universal and infection rates are extremely high.

The bottom line is that there is insufficient evidence that BCG vaccination of South African adults will impact on COVID-19 morbidity and mortality. In addition, there is no evidence to indicate that BCG vaccination is safe in older populations. If we are to consider using BCG in the COVID-19 pandemic in South Africa, then this first needs to be subjected to a clinical trial to generate evidence.

The current mainstay for prevention of COVID-19 remains social distancing, cough hygiene and hand washing.

Reference

Miller A, Reandelar MJ, Fasciglione K, Roumenova V, Li Y, Otazu GH. Correlation between universal BCG vaccination policy and reduced morbidity and mortality for COVID-19: an epidemiological study. medRxiv posted March 28, 2020. https://doi.org/10.1101/2020.03.24.20042937

CHALLENGES IN IDENTIFYING PAEDIATRIC COVID-19 PATIENTS IN AFRICA

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Ever since the first reports of 'an unusual pneumonia' emerged from Wuhan, China on 27 December 2019 and its subsequent introduction to Africa on 14 February 2020, all African countries barring Lesotho have reported affected individuals.[1]

As of 8 May 2020, the African Center for Disease Control and Prevention has reported 54,027 cases of COVID-19 with 18,636 recoveries and 2,074 deaths. While regionally, northern and western African nations accounted for 65% of diagnoses, Egypt, South Africa, Morocco, Algeria, Cameroon, Ghana, Guinea, Cote d'Ivoire, Djibouti, Senegal and Tunisia (all with 1000+ cases) were the countries with the most reports (not necessarily the most affected).[2] The epidemiological statistics should be taken with a pinch of salt as case identification goes hand in hand with the adequacy of diagnostics and contact tracing.

Successive studies from many countries show that children and adolescents are in the minority among affected people. A large Chinese study (more than 72,000 cases) included only 416 cases among children 9 years or less (no mortalities) and 549 in the age group 10 – 19 years (one mortality).[3] As more than 90% of children are asymptomatic or exhibit mild to moderate symptoms, paediatric case detection remains challenging.[4]

Reports depicting the age distribution of patients infected by SARS-CoV-2 in African countries are hard to access. Official outlets of ministries of health and public health institutes do not relay specifics in epidemiologic statistics in a timely and accessible manner.

The median age of the African population is very young at 19.7 years.[5] While this could lead the age distribution of the COVID-19 affected population to be skewed to the youth, thus departing from trends in other continents, the proportion of children under the age of 18 years affected by COVID-19 in the few African countries where data is accessible remains very small, ranging from 0 – 10%.

Country	All patients			Age ≤18 years
	Total cases	Recovered cases	Died	Total cases (deaths)
Botswana	23	8	1	0
Burundi	15	7	1	0
Comoros	8	0	1	0
Djibouti	1008	373	2	0
D.R. Congo	459	50	28	0
Ethiopia	162	93	4	15
Kenya	384	129	15	16 (1)
Lesotho	0	0	0	0
Mauritius	331	266	9	23
Morocco	5219	1838	181	391 (1)
Mozambique	81	12	0	1
Namibia	16	9	0	1
Rwanda	206	110	0	6
Seychelles	11	6	0	0
South Africa	7220	3153	153	334
Uganda	79	46	0	8

Table 1: COVID-19 statistics in Africa, compiled on 7 May 2020. Data sourced from reference 6, except for Ethiopia (Source: Ethiopian Public Health Institute) and South Africa (Source: @HealthZA).

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THE EMERGENCE OF COVID-19: PIECING TOGETHER THE KNOWNS AND UNKNOWNS

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INTRODUCTION

The novel corona virus pandemic has caused devastation to humans, health systems and economies around the world. The world has not seen such a devastation from one single disease in decades. Age old social habits have been broken to reduce the transmission of the virus. For the moment, there is no definite cure or vaccine against the disease. The coronavirus disease 2019 (COVID-19) infection first presented as a cluster of pneumonia cases in Wuhan, China where the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was later identified as the causative organism [1, 2]. Although there are a lot of unknowns about the virus, there are lessons to be learned from similar pathogens and preliminary reports about its pathogenesis, transmission, presentation and management.

The level of preparedness and public health response in different countries are geared towards breaking the chain of transmission and flattening the curve of the pandemic of this emerging highly infectious disease. Apart from the mortality crisis, no other event in the last decades has impacted so negatively on the health system and global economy. Worse still, accusations and counter accusations are rife about the origin and handling of the outbreak among countries. It appears that the effects of the pandemic will last for a long time.

A lot of myths and misconceptions have been propagated about the virus. This has been worsened by the social media explosion of a lot of misleading information on every aspect of the virus. The World Health Organization (WHO) has coined this epidemic of information as "infodemics of COVID-19". One of the myths about the disease is that children and adolescents cannot contract the infection. This write-up aims to piece together the information available about the virus, its effect on some populations and to ponder on life after the emergence of the organism.

EPIDEMIOLOGY

Global estimates put the total number of confirmed cases of COVID-19 infection at almost 4 million with about 300,000 deaths as at 13 May 2020, and still rising [3]. The epicentre of the infection had shifted from China where the infection originated, to Europe and currently is in the United States [3]. As of 13 May 2020, among all the regions, the African region has recorded the lowest figures 72,165 with 2,449 deaths [3]. Nigeria, the most populous African nation, as at 14 May 2020 has recorded 4971 cases with 164 deaths and 1070 discharges. Males accounted for 69%. Most affected age group is between 31 and 40 years (25%). The distribution of cases shows that 4% had a travel history, 23% were contacts of index cases, there was no epidemiological link in 65%, suggesting community transmission and in 8%, the source of infection was unknown. Furthermore, a recent publication of the first 32 cases in Nigeria reveals that children accounted for 12.5% of cases and 75% of all cases were of moderate severity. Does this mirror the African situation? Will this change over time? Though testing has been limited in most African countries, the explanations that have been offered for the low incidence of COVID-19 are numerous and are yet to be proven.

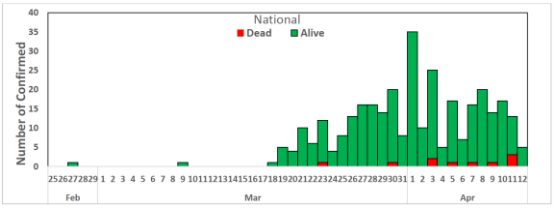

Figure 1: Daily epi-curve of COVID-19 cases in Nigeria (Week 9 – Week 20)

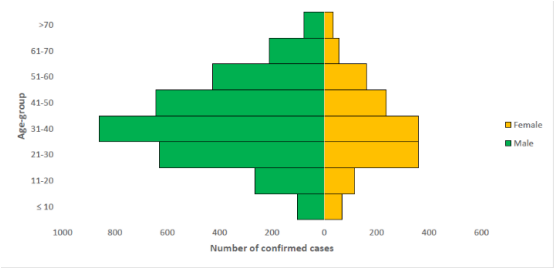

Figure 2: Age-sex distribution of confirmed cases in Nigeria (Source: NCDC) (Week 9 – Week 20)

MODE OF TRANSMISSION

Two main routes of transmission have been identified, namely, droplet and contact with the objects and surfaces in the environment that have been contaminated with the droplets [4, 5]. Airborne transmission is possible, when aerosols are generated during aerosol generation procedures like mechanical ventilation or airway suctioning [4]. There is concern that prolonged suspension of the droplets in the air with potential aerosol transmission may occur. When droplets generated during activities such as coughing and sneezing hang in the air for many hours, this may pose a risk to individuals within the vicinity [6]. Shedding of the virus is reported to be highest in the nose and throat, usually early in the disease process, with similar viral loads in asymptomatic and symptomatic patients [7], supporting the fact that transmission can occur from symptomatic, asymptomatic as well as pre-symptomatic individuals [5, 8]. Like other respiratory viruses such as measles, transmission can occur during this pre-symptomatic period. The incubation period for COVID-19 i.e. the time between exposure to the virus and the onset of symptoms varies, from 1 to 14 days with a median of 5.1 days (95% CI, 4.5 to 5.8 days) with 97.5% of exposed individuals being infected by day 11.5 days [9]. The "Test, test, test" strategy ensuring widespread testing which has been advocated is critical for identifying and confirming positive cases. Just as is applied in some other infectious diseases, COVID-19 can be contained by isolating cases and their positive contacts.

COVID-19 IN INFANTS, CHILDREN & ADOLESCENTS

Infants and children have been spared in the pandemic for the most part, but it is a myth to conclude that children are not affected by COVID-19. Children and adolescents are potential transmitters of the virus. One of the few studies

available on the epidemiology and transmission of COVID-19 in children came from China in which the data of over 2000 cases were analysed. The results showed that the median age was seven years with an interquartile range of two to thirteen years with no significant gender difference. Notably, over 90% of the cases were asymptomatic, mild or moderative. Fewer severe and critical cases (5.9%) were recorded than adult patients (18.5%) [10]. Another study identified nine infants who were hospitalized during the outbreak. Though the inferences from this study were limited by the small number, the authors were able to show that infants could be affected by COVID-19 as the earlier stage of the epidemic primarily involved individuals older than 15 years [11]. The reasons adduced to why the clinical manifestation is mild in children include their immature system which does not respond with the cytokine storm seen in adults, this accounts for the severe and critical disease in them. Also, the receptor which the virus uses for cell entry, the angiotensin converting enzyme 2 receptor, may be expressed differently in children [12, 13]. No vertical transmission of COVID-19 has been documented as maternal vaginal and amniotic fluid, cord blood and neonatal nasopharynx specimens, have consistently tested negative. Infected neonates are likely infected from droplets or close maternal contact [14-18].

The impact of the virus on other aspects of child health is enormous. Routine infant welfare services such as immunization have been disrupted in areas implementing a lockdown. Children under these circumstances may also be prone to increased violence, exploitation and abuse. Many more newborns, children and adolescents could be lost to non-coronavirus related causes when the health system is overwhelmed. School closures have disrupted the education of millions of children.

COVID-19 AND HIV INFECTION

Little is known about the interphase of HIV and the coronavirus. There remains the question as to whether individuals with HIV are at increased risk of COVID-19 infection. Available data do not suggest increased risk of infection or severe forms of COVID-19 among HIV infected individuals if they are on antiretrovirals and virally suppressed [19]. However, it is to be expected that the presence of co-morbidities in HIV infected individuals will pose a risk for more severe disease. Similarly, for those with a low CD4 count (<200 copies/µL), a high viral load, or a recent opportunistic infection there is increased risk of infection and severe COVID-19 [20]. However, delayed immune response and viral clearance in COVID-19 among HIV co-infected individuals is suggested [21]. People living with HIV infection might experience antiretrovirals supply challenges and are advised to stock up while adhering to all the recommended measures.

DIAGNOSIS

Clinical features

Most infections in children are mild and self-limiting. More severe illness is seen in elderly population or in patients with underlying medical problems [22]. More severe disease and poorer outcomes have also been reported in infants and children with co-morbidities such as sickle cell disease, diabetes and obesity. The most common presentations in children are fever and cough [13]. Other symptoms of COVID-19 in children include, fatigue, sore throat and difficulty in breathing, headache, muscle pain. There may also be non-respiratory manifestations with features of diarrhoeal disease alone. The severity of the disease can be categorised into asymptomatic infection in which there are no clinical symptoms or signs and the chest imaging is normal. Mild cases show symptoms of acute upper respiratory tract infection such as fever, fatigue, myalgia, cough, sore throat, runny nose, and sneezing. In some cases, fever may be absent but there may be only digestive symptoms such as nausea, vomiting, abdominal pain and diarrhoea. Moderate cases present with pneumonia. In severe cases, early respiratory symptoms such as fever and cough, may be accompanied by gastrointestinal symptoms such as diarrhoea. Respiratory distress is present with desaturation. In critical cases, the patient progresses to acute respiratory distress syndrome (ARDS) or respiratory failure, and may also have shock, encephalopathy, myocardial injury or heart failure, coagulation dysfunction, and acute kidney injury. Organ dysfunction can be life threatening.

Of interest are recent reports of a Kawasaki-like syndrome in children in Europe and the USA [23, 24]. These have been documented in both COVID-19 positive and negative children. The clinical presentation, including cardiac involvement, and treatment mirrors Kawasaki disease albeit the incomplete form. The seasonality and increased frequency in these areas are quite unlike classic Kawasaki [23, 24]. As with Kawasaki, the aetiology remains unknown. There has been suspicions that Kawasaki is related to coronavirus infection or other infectious inflammatory triggers. Does COVID-19 have a role to play in this emerging syndrome? Many more questions remain unanswered regarding the COVID-19 pandemic.

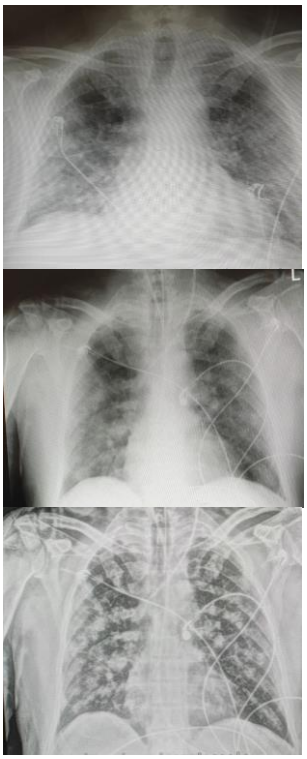

Figure 3a, b and c: Progressive lung parenchymal damage in COVID-19 infection

Laboratory testing

The role of the laboratory in the pandemic is to confirm the infection in suspected cases, screen for the virus among contacts of the cases and map the extent of spread of the infection, whether clusters exist and the extent of community transmission. Laboratory testing is also used to monitor clearance of the infection in previously confirmed cases. When targeted testing is done as is the case in many countries where limited test kits exist,

asymptomatic individuals are likely to be missed. The implication is that the reported cases are an underestimation of the actual number of cases. The estimated number of infections was found to be on average about 9 times higher than the recorded number of infections in an Austrian study [25]. This is also probably the case in most low- and middle-income countries where testing lags significantly behind high resources settings due to limited resources [3].

Specimens to be collected include oropharyngeal swab, nasal swabs and sputum (if it can be produced), while trachael aspirate or bronchoalveolar lavage is recommended if the patient is intubated. Saliva is also being considered as it has been found to have a high yield of the virus. The infection can be detected by testing for viral RNA using real-time reverse-transcriptase polymerase chain reaction (RT-PCR) assays. The sensitivity of 1070 different clinical specimens were analysed from 205 hospitalised patients and showed that BAL had the highest positive rates of 93%, sputum 72%, nasal swab 63% and, pharyngeal swab 32%. The least yield was from blood. It was recommended that testing of specimens from multiple sites increase the sensitivity [26]. The turnover time for the PCR test varies from 24 hours to one week. During this time lag, the infected individual may continue to spread the virus if appropriate infection control measures are not put in place.

Rapid point-of-care antibody tests have become available. The rapid test uses the principle of lateral flow immunochromatography and detects either IgM, IgG or IgA and can be used for the screening for exposure to the virus in hospitals, clinics, and test laboratories. The accuracy of the antibody tests has remained an issue. The IgM-IgG combined assay has better utility and sensitivity compared with a single IgM or IgG test. Apart from testing for who has been exposed, it can also reveal that an individual has mounted immunity to the virus. Whether the evidence of antibodies translates to protection against a reinfection remains to be seen. However, antibody tests, applied at the population level, has the potential to define, properly, the scale of the epidemic. Antigen based tests have also become available, though sensitivities are less than NAT based test. They are potentially useful bridges, especially in resource constrained settings, as they are point-of-care tests, cheaper, results available in about 15 minutes and require less technical expertise in performing. Most use the lateral flow assay template [27].

Genetic sequencing of respiratory tract or blood samples have been used to trace COVID-19 sources. In a recent study, a phylogenetic network analysis of 160 complete human severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) genomes, three central variants were found distinguished by amino acid changes, which have been named A, B, and C representing the different sources [28]. Other supportive laboratory evidence for COVID-19 are leukopenia with lymphopenia, elevated alanine transaminase, increased D-dimer, procalcitonin, C-reactive protein and ferritin.

TREATMENT

Currently, there is no definite treatment for COVID-19 infection. Supportive care is the main stay of management. The clinical management of COVID-19 cases would be based on the severity of the disease. Patients are closely monitored with the level of care being escalated with increasing severity of symptoms. Pre-morbid conditions which increase the risk of progression of the disease must be assessed and appropriate management instituted. Complications are managed as necessary. The discharge of a patient should be based on clinical grounds and supported by laboratory results showing negative PCR such that the virus can no longer be detected in the respiratory samples [29].

Many antimicrobials are being used either alone or in combination therapies for the treatment of COVID-19 infection. Examples of pharmacological therapies that have been used include hydroxychloroquine/chloroquine alone or in combination with azithromycin, lopinavir/ritonavir (kaletra), remdesivir and tocilizumab. Outcomes of the efficacy and safety clinical trials of many of these therapies are conflicting and others are being awaited [30]. The evidence for use of these agents had largely been limited in most instances by small numbers, confounding co-interventions, insufficient measurements of outcomes and other methodological bias [31]. Clinical progression and virologic clearance should be the goal of any optimal therapy. Recent preliminary evidence from a multi-country randomized controlled trial of remdesivir among severe cases of COVID-19 showing promise with a statistical reduction in length of hospital stay from 15 days to 11 days and a trend towards significant reduction in mortality from 11.6% to 8% [32].

PREVENTION

The infection, prevention and control measures for COVID-19 transmission begins with hand hygiene which encompasses hand washing with soap and running water or use of alcohol rub or hand sanitiser. Hand hygiene has been described as the single most effective way of preventing diseases spread by contact. Other public health practices that have been adopted containing the COVID-19 pandemic include quarantine, self-isolation, social distancing and lockdown. While quarantine separates and restricts movement of individuals that have been exposed to the infection to see whether they will develop the symptoms, isolation refers to separating symptomatic individuals from those that are healthy. Contacts of persons confirmed with COVID-19 are quarantined for 14 days from the last time they were exposed to the patient. Whether individuals are quarantined or isolated in the context of an infectious disease, they are monitored regularly for symptoms of the disease. Widespread testing is recommended for suspects and their contacts as a means of identifying and isolating positive cases for appropriate isolation measures.

Physical or social distancing means that people should keep a minimum distance of 2 metres from one another. Cough etiquette is also advocated just as for other airborne infections like tuberculosis, whereby someone coughing, or sneezing covers their cough, using a disposable tissue and discarding in a waste bin and washing their hands or using their bent elbow. During a lockdown, restriction of routine activities is implemented to different degrees by different settings. With total lockdown, only essential services are permitted to be carried out. The WHO has recommended the conditions that must be met for ending a coronavirus lockdown which includes among others, ensuring that the disease transmission is under control and the health system is able to detect, test, isolate and treat every case and trace every contact. Communities are fully educated, engaged and empowered to live under a new normal.

One of the raging controversies about prevention of the infection is the universal use of masks. Important issues to be considered when deliberating on the use of masks include the type of mask to be used, type of transmission in the setting (clusters or community spread), use by a healthy versus symptomatic individual, the setting – whether in the community or in the healthcare setting, and the availability of the masks. Different types of masks have been used whether appropriately or inappropriately with the view to limiting the spread of COVID-19 infection.

Respirators (N95 masks) filter 95% of microorganisms are to be worn by health care workers managing patients with risk of airborne infections. While surgical or procedure masks are indicated in patients and health care workers with respiratory infection, or in health care workers at risk of droplet infection when providing care near infected or potentially infected patients.

There is evidence that wearing a surgical mask by a person with respiratory diseases can prevent the spread of infectious droplets from an infected person to someone else and potential contamination of the environment by these droplets [33]. No such evidence of prevention exists currently for the use of any type of masks by healthy individuals in the community setting. The WHO therefore warns that the use of a mask alone is insufficient to provide an adequate level of protection, and other measures should also be adopted. Whether or not masks are used, maximum compliance with hand hygiene and other IPC measures is critical to prevent human-to-human transmission of COVID-19 [34].

The problems that are associated with inappropriate mask use include self-contamination that can occur by touching and reusing contaminated mask, breathing difficulties, a false sense of security with less adherence to other preventive measures such as physical distancing and hand hygiene, diversion of mask supplies and consequent shortage of masks for health care workers, and diversion of resources from effective public health measures, such as hand hygiene. It is therefore advocated that when masks are worn, all additional preventive measures are adopted, particularly, hand hygiene and maintaining physical distance from other persons.

With regards to vaccines, more than 100 vaccines are under development. Presently only 3 are at the early phases of clinical evaluation. The WHO has developed a document that describes the preferred minimally acceptable profiles for human vaccines for long term protection of persons at high ongoing risk of COVID-19 and for reactive use in outbreak settings with rapid onset of immunity. The Target Product Profile (TPP) is a collaboration of key stakeholders in human and animal health, scientific, funding and manufacturing communities [35].

LIFE AFTER THE EMERGENCE OF COVID-19

Is this a virus that will co-exist with humans on the planet? Two end points are envisaged. Global efforts of containment could result in the break in transmission of the virus or the virus eludes elimination. If the virus is not eliminated, it may then go on to cause sporadic infection or periodic outbreaks in the population when the conditions are conducive. If the latter is the case, the world must then learn to live with the virus.

Should there be a concern about reactivation or recurrence (re-infection)? Can false negative tests explain the cases of testing positive again after being thought to clear the virus? Or is the virus capable of hibernating in sanctuary sites as is seen in HIV infection? The salivary glands have been suggested as the potential reservoir for COVID-19 asymptomatic infection [36]. Immunity after the natural infection is not assured. But going by other corona viruses, any immunity after a natural infection is likely to be short lived, possibly for a few months, but providing prompt immune response with subsequent exposure and ensuring a milder disease course.

Children and adults alike have suffered devastating consequences from the effects of the COVID-19. Routine infant welfare services need to continue with appropriate infection control measures such as strict hand hygiene as well as physical distancing at the immunization centres. Are lockdowns the new normal and how will child health services adapt to this? Will this further worsen the disparities in health between the low and middle income and the more resourced countries who better equipped to adapt?

Will social habits such as shaking hands and hugging that endear us to one another as humans, become a thing of the past? Currently, the world appears to be better connected than ever through cyber space with lots of virtual learning and other interactions. But would virtual learning fill the gap for skills that are meant to be acquired practically by physical demonstration and contact with instructors? Furthermore, if a lockdown is maintained for a prolonged period, children in less developed settings where internet facility is lacking would be disadvantage with the continued shutdown of class work. The effect of the pandemic on the economy is already evident in most affected countries. When will the economy recover? Though countries in Africa have a lower incidence of the infection, health systems and programmes in the region depend largely on external funding sources. There may be reduced donor support and other indirect economic effects of the pandemic in Africa. Time would tell as the answers to these questions gradually unfold.

CONCLUSION

As the outbreak continues to evolve, with many unanswered questions, it is important to seek information from reliable sources for the appropriate response to the virus. Increased testing is the way to identify infected individuals such that appropriate isolation can be carried out to break further transmission while effective therapy and vaccines are awaited. Many aspects of human lives have been affected by the pandemic. Indeed, COVID-19 has changed our world forever.

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CURRENT DIAGNOSIS & MANAGEMENT OF VISCERAL LEISHMANIASIS AND CHALLENGES IN ETHIOPIA

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INTRODUCTION

Leishmaniasis is one of the tropical diseases that affect mainly the poorest people on earth. The disease is associated with malnutrition, population displacement, poor housing, a weak immune system, and a lack of financial resources.[1] Visceral leishmaniasis (VL) or 'kala-azar,' a severe form of the disease, is endemic in many developing countries. The disease is highly endemic in East Africa and the Indian subcontinent (ISC), globally around 50 000 to 90 000 VL cases, new, occur annually with only between 25 to 45% reported to WHO.[2] In 2018, more than 95% of new cases reported to WHO occurred in 10 countries: Brazil, Ethiopia, India, Kenya, Nepal, Iraq, Somalia, South Sudan, China, and Sudan.[2]

The transmission and epidemiology of the disease are complicated due to the complex life cycle of the parasite and the involvement of various sand fly vectors and reservoir animals besides human hosts. [3-5] The etiological agent of human VL in the Old World is represented by two closely related parasite species belonging to the *Leishmania donovani* complex. These are, *Leishmania infantum* which circulates as a zoonosis, with domestic dogs and wild canids as the main reservoirs[3], and *Leishmania donovani*, which is believed to be anthroponotic and mainly transmitted among humans.[4] *Leishmania donovani* is the cause of VL in ISC and East Africa.[6] Rodents have been reported as a reservoir in several VL endemic countries caused by *L. donovani*[7]; however, the status of rodents as reservoirs in East Africa remains unclear. However, a recent study from Ethiopia demonstrated natural *L. donovani* infections in rodents.[5] This finding indicates that rodents can have an essential epidemiological role in the transmission cycle in East Africa though it needs further study.

Visceral leishmaniasis is characterized by several complexities, and its clinical features are often confused with other febrile illnesses. Besides, misdiagnosis may exist with patients having less clinical manifestations or atypical presentation, causing a delay in treatment and thus leading to the death of patients. To address this real challenge in clinical care settings, rapid and accurate confirmatory diagnostic tests are needed as anti-leishmanial drugs can cause significant adverse reactions.[8] In East Africa, parasitological diagnosis remains the reference standard in VL diagnosis, typically undertaken by microscopic confirmation of parasites in tissue aspirates.[9] However, it is not possible to apply this standard at scale in remote areas that lack even the most basic laboratory set-up.[9] The rK39 rapid diagnostic test is widely used as a confirmatory test in India with very high accuracy, but sensitivity issues have severely limited its usefulness in the African continent.[9] The disease is fatal in more than 95% of cases if left untreated within two years after the onset of the disease.[1] Currently, available therapies have serious drawbacks: most of them have serious side effects and are administered for a pronged period, other therapies are expensive and there are concerns of drug resistance.

In the ISC, three countries affected by VL, India, Nepal and Bangladesh aspire to eliminate VL from the subcontinent starting from 2005, through various control measures.[1] Since 2007 the incidence of visceral leishmaniasis in the region has fallen sharply and in 2015 had reduced by 82%.[1] One of the crucial components in this effort is decreasing transmission through early diagnosis, followed by complete treatment. Similarly, in East Africa, the Leishmaniasis East Africa Platform (LEAP) is working with stakeholders from countries in the region to address the specific needs of the area, such as using effective drug combinations, availability of less toxic drugs and more affordable shorter course.[10] Despite these efforts, the disease remains a significant problem in East Africa as many patients are not getting treatment on time as the service is not decentralized, and relapse and drug resistance are challenges, particularly among HIV-infected patients.[1,8]

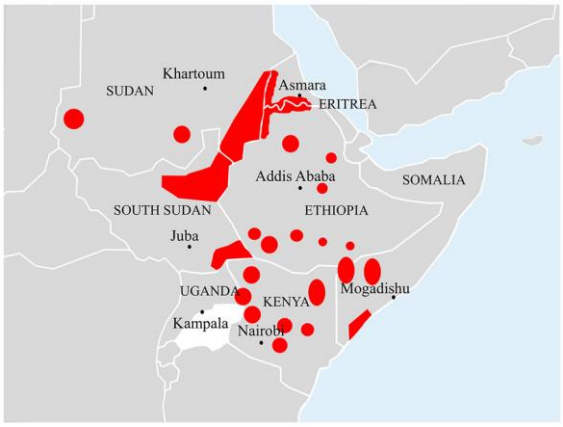

Figure 1: Geographical distribution of Visceral Leishmaniasis in East Africa

VISCERAL LEISHMANIASIS IN ETHIOPIA

Visceral leishmaniasis is one of the growing public health challenges in Ethiopia, with over 3.2 million people at risk and up to 4000 new cases occurring per year.[11] The predominant climate type in Ethiopia is tropical monsoon, with a temperate climate on the plateau and hot in the lowlands. There are topographic-induced climatic variations broadly categorized into three: the "Kolla," or hot lowlands, below approximately 1,500 meters, the "Wayna Degas" at 1,500-2,400 meters, and the "Dega" or cool temperate mountains above 2,400 meters.[12] In Ethiopia, VL was known as the disease of the lowlanders occuring in the lower & upper kola agro-ecological zones. Some of the areas known to be endemic are Metema and Humera plains in the northwest, several localities of southwestern region, southern Ethiopia around Moyale area close to the borders of North Kenya, and Hamar and Banna-Tsamai, southeast around Genale river basin, Raya Azebo in the northeast & Benishangul Gumuz regional state in the west.[11,13] However, since the 2005-2007 outbreaks in the highlands of Libo Kemkem and Fogera, and Wayna Degas, indicate the establishment of VL transmission in the highlands adjacent to the lowlands.[14] The kola & Woina Dega are the most productive agro-ecological zones, supporting both the ongoing and planned expansion of large or small scale agriculture and/or agricultural-based industries in Ethiopia. Thus, VL is not only a public health & social problem but also has direct implication on the country's economy and future development.

CURRENT DIAGNOSTIC CHALLENGES

Early and accurate diagnosis is essential as VL is fatal if left untreated and because the available drugs are potentially toxic and expensive. Furthermore, untreated individuals might act as reservoirs putting the community at risk of ongoing transmission. Therefore, early detection and proper management are crucial for control of this disease. The current diagnosis of VL is based on clinical presentation plus serology and / or parasitology according to the national guidelines.[11] Currently, molecular tests are only used in research studies.

Clinical diagnosis is based on the standard case definition of VL i.e. a person who presents with fever for more than two weeks, an enlarged spleen (splenomegaly) and/or enlarged lymph nodes (lymphadenopathy), or either loss of weight, anaemia or leucopaenia while living in a known VL endemic area or having travelled to an endemic area.[11] This case definition lacks specificity as the disease mimics other febrile illnesses or non-infectious diseases due to late presentation. Therefore, a definitive test is required to confirm the diagnosis.

Antibody tests: Among the different serological tests that have been developed for VL, the direct agglutination test (DAT) and rk39 rapid diagnostic test (RDT) have been extensively validated in *L. donovani* endemic areas and recommended for use in VL control programmes, including in Ethiopia.[15] However, both tests cannot discriminate between current, subclinical, or past infection and therefore is not useful for diagnosing relapse disease or for monitoring treatment response.

rK39 rapid diagnostic test (rK39 RDT): In Ethiopia, the use of the rK39 RDT, based on the recombinant K39 protein antigen, is recommended for all patients who meet the case definition.[11,16] The test is reproducible, economical, easy to perform, and can provide a result within 10 - 20 minutes.[17] These features make it an ideal diagnostic tool for peripheral health facilities in VL endemic localities. However, the response of rK39 RDT is less effective in East Africa (Sudan and Ethiopia), demonstrating sensitivities between 70% and 94%. In the ISC, the test has high diagnostic accuracy.[18] The lower sensitivity of the rK39 dipstick in Ethiopia highlights the need for careful monitoring and the development of new generation diagnostic kits with better sensitivity. For the above reasons, the national guidelines recommend that DAT, a more sensitive test, be performed if the rK39 RDT yields a negative test result. Visceral leishmaniasis treatment should be started if the rK39 RDT is positive unless relapse infection or re-infection is suspected.

Direct agglutination test (DAT) is a semi-quantitative test that uses a microplate with V-shaped wells, in which increasing dilutions of patient serum or blood are mixed with killed and stained freeze-dried or aqueous *L. donovani* promastigotes. Agglutination can be seen with the naked eyes after overnight incubation if specific antibodies are present. The performance of DAT as a diagnostic test is satisfactory, relatively economical, and independent of geographical region.[19] DAT has been validated in several countries and has better sensitivity comparing to rK39RDT in the Ethiopian setting.[11,19] The national guidelines recommend doing this test in suspected cases in which the rK39 RDT result is negative. However, the test is not available in many primary health care facilities (PHCs) in the country as it requires electricity, storage of antigens at 2–8◦C, multiple pipetting, and skilled personnel.

Parasitological Diagnosis: Parasite detection is the gold standard diagnostic test for VL. Diagnosis is confirmed by visualization of the amastigote form of the parasite by

microscopic examination of aspirates from lymph nodes, bone marrow or spleen. The sensitivity of microscopy varies: 93 - 99% for spleen, 53 - 86% for bone marrow, and 53 - 65% for lymph node aspirate.[11,19] Splenic aspiration remains the most specific method of diagnosis in practice in Ethiopia, as in other East Africa countries. Splenic aspiration is recommended if rK39RDT is negative & DAT borderline or not available. The parasitological test is also the only confirmatory test that exists for relapse patients. However, the test requires highly trained personnel for performing splenic aspiration and high-powered microscopy. Aspiration can be associated with complication due to the invasive nature of the procedure. Hence, it is not practical at the PHC level.

In the 2012 World Health Organization (WHO) roadmap, a target for VL is the achievement of 100% case detection and treatment.[1] This target can only be realised if rapid, cost-effective, less invasive and more sensitive diagnostic tests become available in disease-endemic countries such as Ethiopia. However, this doesn't seem to be possible before the by the end of 2020.

CURRENT MANAGEMENT OF VL AND DIAGNOSTIC CHALLENGES

Visceral leishmaniasis is the most neglected tropical disease, particularly in terms of new drug development because of lack of financial returns. The use of high-quality drugs is not only a therapeutic tool but also an essential strategy for VL control due to the anthroponotic nature of the transmission of *L. donovani* in Ethiopia.

First-line Regimens for VL: Since 2010, the combination of sodium stilbogluconate & paramomycin (SSG & PM) has been recommended by WHO as first-line treatment for VL caused by *L. donovani* in East Africa.[20] The Ethiopian treatment guidelines also recommend that a 17-day course of the combination of SSG & PM be used as first-line treatment for VL if both drugs are available.[11] A recent systemic review by Gebreyohannes EA et al. showed that the efficacy of the combination of SSG & PM is better than SSG monotherapy, with the advantage of decreased toxicity, shorter treatment duration, and cheaper cost.[11,21] This finding makes it rational to use SSG & PM as first-line medication in the country. During stock-outs of paromomycin, SSG can be used as monotherapy for 30 days though it is associated with significant side-effects. Liposomal amphotericin B (L-AmB, AmBisome) is the first-line treatment for VL in special situations, notably in pregnancy, HIV co-infection, severe illness, severe anaemia, severe malnutrition and at the extremes of age (below two years or above 45 years).[11] Unlike in the ISC, single-doses of L-AmB has low efficacy and should not be used in Ethiopia, whereas multiple doses ((≥ 6 doses) of L-AmB has excellent efficacy.[21]

Second-Line Treatment for VL: Indications for the use of second-line VL treatment are drug toxicity, relapse disease, treatment failure, very severe illness, pregnancy, and VL/HIV co-infection. The second line treatment for VL in Ethiopia is L-AMB. Besides its high therapeutic index, AmBisome has a relatively short treatment course and minimal side effects; its main disadvantage is its high cost.

In general, treatment options for VL in Ethiopia has increased in the past two decades with the successful works of LEAP, including clinical trials that showed the combination of SSG & PM is safe and effective as SSG monotherapy.[22] However, available options are still limited, and they have problems related to efficacy, adverse effects, drug resistance, high cost, and need for hospitalization. Hence, it is crucial to safeguard the effectiveness of these drugs by availing an uninterrupted supply of quality drugs, promotion of treatment adherence, and monitoring of treatment effectiveness as well as drug resistance. As a short-term solution, Drugs for neglected tropical diseases (DND) & LEAP are also looking for better combination treatment regimens using existing drugs.[22]

VL/HIV CO-INFECTION

Human immunodeficiency virus (HIV) affects VL incidence, alters its clinical manifestations, causes diagnostic challenges, significantly decreases treatment responses and is associated with increased relapse rate.[23] At the same time, VL promotes the clinical progression of HIV infection and the development of AIDS-defining conditions as the two diseases target similar immune cells. For this reason, VL is considered a WHO stage 4 or AIDS-defining illness. HIV-VL co-infected patients are chronically infected, frequently suffer relapse episodes with high parasitaemia, and act as a major *L. donovani* reservoir in the population.[24] Ethiopia has the highest HIV-VL co-infection burden globally, ranging between 20–40%.[25] Young male seasonal workers who migrate to the lowlands of the northwest of Ethiopia for work are particularly at high risk.[25]

HIV-infected patients with advanced immunosuppression (very low CD4+ T-lymphocyte counts) may present with atypical clinical manifestations. The sensitivity of serological tests is low in such cases.[26] Thus makes VL diagnosis difficult in HIV-infected patients based on clinical presentation plus serology. Therefore, the gold standard for the diagnosis of leishmaniasis in HIV-infected patients is the identification of the parasite in on splenic, lymph node, or bone marrow aspirates. However, this diagnostic approach is not possible in most PHCs.

The Ethiopian national guidelines recommend liposomal amphotericin B and SSG as the first- and second-line treatment for HIV-VL patients, respectively.[11] This recommendation is in line with the current WHO recommendation of AmBisome with a total dose of 40 mg/kg body weight (high dose) administered in divided doses for the treatment of VL-HIV co-infected individuals.[20] The effectiveness of AmBisome at 30 mg/kg was less than 60% among HIV co-infected patients, but there are no studies using 40 mg/kg.[27] Sodium stilbogluconate therapy also has poor effectiveness (43%–70%), significant toxicity and high risk of death among such patients.[28] Overall, the treatment outcome of HIV-VL co-infection with all currently available anti-leishmaniasis treatment regimens is poor. A recent clinical trial by Diro E et al. using a combined regimen of AmBisome [30 mg/kg total dose of AmBisome was administered according to the following schedule: IV slow infusion of 5 mg/kg on days 1, 3, 5, 7, 9, and 11] and miltefosine [50 mg capsule orally twice a day for 28 days] in patients with a bodyweight >25 kg achieved a parasite clearance rate of 81% at the end of treatment (the primary outcome) with high compliance and satisfactory safety profile.[29]

Implementation of this regimen can also enhance parasite clearance at the community level by reducing the circulation of the parasite as HIV-infected patients have chronic infection with high parasitaemia. Results of this study and another similar trial on HIV/VL co-infected patients from India will be reviewed this year, 2020, by a WHO Guideline Development Group evaluating treatment recommendations for people co-infected with VL and HIV.[22] If the evaluating team supports the use of the combination treatment, it may be included in the national treatment guidelines as the first-line regimen for HIV-VL co-infected patients in Ethiopia and other African countries in the region.

The profound immune deficiency in HIV/VL co-infection results in frequent recurrences of VL. In northwest Ethiopia, where the HIV co-infection rate is the highest in the world, relapse reaches as high as 56% in a year in patients on ART but without secondary prophylaxis.[30] Therefore, preventing relapse of disease is very important as such cases are difficult to cure, become reservoirs of the parasite, and play a role in transmission.[24] Currently, there is no secondary prophylaxis recommended by Ethiopian national guidelines. A recent cohort study in Ethiopia demonstrated 71% disease-free survival one year after VL treatment using pentamidine as secondary prophylaxis.[31] However, patients with a profound immune deficiency were still at risk of relapse and the study had several limitations, including methodological problems. Hence, there is a need for further research on the efficacy and safety of higher doses of pentamidine and optimal HIV care in this group of patients.

POST-KALA-AZAR LEISHMANIASIS

Post-kala-azar dermal leishmaniasis (PKDL) is a skin complication that occurs in patients who have recovered from VL. This condition occurs in 50–60% of patients mainly from Sudan, and to some extent Ethiopian patients are affected.[32] The condition appears within weeks to a few months after treatment. Clinical features consist of hyperpigmented macules, diffuse infiltration, papules, nodules, or plaques and can be confused with other skin disorders. The only confirmatory test is skin slit smear microscopy, but it is very painful and impractical with macular lesions.[33] As PKDL patients harbour the parasite they can be potential sources of infection and disease transmission. Hence, patients should be advised to seek medical attention and use impregnated bed nets if they develop skin rash following VL treatment. Indications for treatment in Ethiopia are severe (grade 2 and 3) lesions, disfiguring disease, lesions that have existed for more than six months, concomitant anterior uveitis/conjunctivitis, and young children with oral lesions that interfere with feeding. Otherwise, most of the lesions heal spontaneously within 12 months, unlike PKDL in India, which takes a longer time to self-heal.[11, 32]The Ethiopian guidelines recommend SSG at least for 30 days until lesions are flattened or are no longer palpable, sometimes longer treatment courses are needed. There are no parasite criteria for cure due to the difficulties of demonstrating the parasite in the lesions. Therefore, non-invasive and rapid point-of-care diagnostic tests are much needed as focal VL outbreaks have been linked to an index case of PKDL. [34]

CONCLUSION

The current VL diagnosis and treatment in Ethiopia has many challenges. The RDT cannot discriminate between current and past infections and does not help for diagnosing relapses and monitoring treatment response. However, parasitological tests are associated with fatal complications and require considerable clinical skill. The available drugs are also injectables (painful and not user-friendly), costly, with high toxicity and inferior efficacy for HIV co-infected VL patients. There is a clear need to fill the gap between current practice, available technology and research for improved VL diagnostics and treatment options.

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CHILDHOOD IMMUNISATION IN THE CONTEXT OF THE COVID-19 PANDEMIC: LEAVING NO AFRICAN CHILD BEHIND

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ABSTRACT

The African continent consists of 55 countries, 47 of which belong to the WHO Regional Office for Africa and 8 countries to the Eastern Mediterranean WHO Office but are united through the African Union. With a rapidly growing population estimated at 1,063,740,000 (14% global population) in 2018, the continent has a large population of persons eligible for immunisation who unfortunately remain unreached. The large pool of unimmunised children, low or declining immunisation coverage rates in some countries and high prevalence of vaccine preventable diseases in African countries indicate an inability to deliver on the commitments of the leaders to immunise all African children, wherever they are. This situation has deteriorated further with the coronavirus 2019 (COVID-19) pandemic which has affected all continents including 54 African countries and negatively impacted on all facets of life. The threat of outbreak of vaccine preventable diseases even with the COVID-19 pandemic makes it mandatory to sustain immunisation and vaccine preventable diseases related services. This paper reviews the situation in Africa and recommends the active participation of various stakeholders in sustaining immunisation services in African countries. The WHO's and other guidelines for immunisation during COVID-19 should be adopted and adapted to local situations for optimal service delivery in each country. Financial, human and other resources are required for effective immunisation and related services during and after the pandemic. Integration of immunisation and COVID-19 services would result in optimal resource utilisation. African children can and should be immunised wherever they are!

INTRODUCTION

The African continent consists of 55 countries united together in the African Union and divided into five regions - Central, Eastern, Northern, Western and Southern Regions with 47 countries served by the World Health Organization Regional Office for Africa (WHO AFRO) and the others by the Eastern Mediterranean Office.[1,2] The member countries of the African Union ratified one of the Sustainable Development Goals' target of ensuring universal health coverage which includes ensuring access to immunisation in recognition of the fact that health is fundamental to social and economic development.[3,4] Despite this ratification and the endorsement of the Global Vaccine Action Plan which aims at universal access to immunisation by 2020, Africa is largely off track in the attainment of its targets as shown in Table 1.[5-8] Sadly, the continent like others, is contending with the evolving and rapidly spreading pandemic of the novel coronavirus (COVID-19) which has impacted on global economy, health and development. The pandemic also threatens to cause reversal of previous gains in immunisation coverage thereby increasing susceptibility to vaccine preventable diseases.[1,2,9] This review paper harnesses information on immunisation in the continent with a view to advocating to stakeholders to sustain immunisation coverage during and after the pandemic.

	Global	Africa
Population statistics		
Total population	7,586,693,000	1,063,740,000
Live births	139,677,000	37,080,000
Surviving infants	135,636,000	35,240,000
Population <5 years	673,691,000	167,675,000
Population <15 years	1,957,802,000	447,507,000
Females, 15-49 years	3,857,865,000	508,857,000
Vaccine-preventable disease: number of reported cases		
Diphtheria	16,651	1,971
Measles	359,921	125,426
Mumps	499,512	54,482
Pertussis	153,631	14,001
Polio	104	65
Rubella	26,006	11,787
CRS	499	18
Neonatal tetanus	1,803	1,130
Tetanus (total)	15,103	5,235
Yellow fever	2,064	734
Percentage of target population vaccinated (WHO/UNICEF estimates)		
BCG	89	80
DTP1	90	84
DTP3	86	76
Hep B – birth dose	42	4
Hep B3	84	76
Hib3	72	76
IPV1	72	62
MCV1	86	74
MCV2	69	26
PCV3	47	73
Pol3	85	74
RCV1	69	32
Rotavirus	35	48
TT2plus	72	74
YFV	49	51

CRS = Congenital rubella syndrome, BCG = Bacillus Calmette–Guérin (BCG) vaccine, DTP = Diphtheria, tetanus, pertussis vaccine, Hep B = hepatitis B vaccine, Hib = *Haemophilus influenzae* type B conjugate vaccine, IPV = inactivated polio

vaccine, MCV = measles containing vaccine, PCV = pneumococcal conjugate vaccine, PoI = polio vaccine, RCV = rubella containing vaccine, rotavirus = rotavirus vaccine, TT = tetanus toxoid vaccine, YFV = yellow fever vaccine

Table 1: The Global and African Immunisation profile in 2018, updated in July 2019 (7,8)

IMMUNISATION IN THE AFRICAN REGION

Immunisation, the process of making a person immune or resistant to an infectious disease, has been adjudged one of the most cost-effective public health interventions in recent times, estimated to save the lives of about 2-3 million each year.[10,11] Sustained immunisation programmes over decades have resulted in increased immunisation coverage rates and reductions in morbidity and mortality from vaccine preventable diseases. For example, WHO reported a 73% reduction in measles deaths in 2018.[12]

As part of efforts to improve immunisation coverage rates, the World Health Assembly approved the Global Vaccine Action Plan (GVAP), a framework mandated to work towards the attainment of the Decade of Vaccines (2011-2020) vision of delivering universal access to immunisation. The attainment of the GVAP's mission of "extending by 2020 and beyond the full benefits of immunisation to all people, regardless of where they are born, who they are, or where they live" requires adequate resources, development of supportive health systems and infrastructure, and capacity development for health workers required to reach remote and marginalised populations.[5] In the last year of the decade, it has been estimated that nearly 20 million children are still unimmunised or partially immunised with over 8 million (44%) being African. In addition to these unreached children, some countries that previously reported high coverage rates have reported that immunisation coverage has fallen, with as much as 10% drop in the rates in 19 countries of which five are in Africa. The reasons for this drop include complacency, lack of investment in public health, conflict, and in some places lack of trust in vaccines.[6,13]

In addition to these challenges, the population of Africa is increasing rapidly thereby increasing the number of children requiring immunisation. It is therefore not surprising that emergencies disasters and epidemics in African negatively impact on immunisation coverage rates leaving many children vulnerable to disease outbreaks. For instance, in the Democratic Republic of Congo in 2019 where the Ebola epidemic infected about 3,400 people and killed 2,200, there was cessation of immunisation services with a resultant outbreak of measles that infected 341,000 people and killed 6,400.[14] Sadly, as the 10th Ebola epidemic in DRC was ending, the 11th epidemic began which has necessitated priority for continued epidemic control efforts to the detriment of immunisation services.[15]

In recognition of its situation, leaders of the African Union have committed themselves through various activities, declarations and resolutions to optimal immunisation services to ensure that all children wherever they are, receive essential life-saving vaccines.[3-5,9,13,16-20] Many of these targets were not attained and those set for attainment by 2020 may not be reached because of the effects of the indirect COVID-19 pandemic on immunisation programmes.[7,8] However, it is expected that the strategies for their attainment can be revised in line with the demands of the current pandemic in 2018 to ensure optimal protection of children and those at risk.

COVID-19 PANDEMIC AND THE AFRICAN CONTINENT

Coronavirus disease 2019, a severe acute respiratory disease caused by a new coronavirus, severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) is a highly infectious communicable respiratory disease first reported in Wuhan city in Hubei Province in China in December 2019. It was declared an emergency by WHO on 30 January 2020 and a pandemic on 11 March 2020. From the outbreak site in China, it has rapidly spread to become a pandemic, involving all continents and almost all African countries. Initially a zoonotic disease, person-to- person spread has become the main mode of the spread of the virus. The number of new cases, deaths and recovered cases change so rapidly and likewise the surveillance report for each day / week. As at June 2, 2020, WHO AFRO reported that 54 countries had been affected with 150, 610 cumulative cases, 4,281 deaths and 63,385 recoveries with South Africa being the most affected with 34, 357 people affected.[1,2,9] The global and African region situation as at June 1 and May 26, 2020 are presented in Table 2. In response to the pandemic, the centres for disease control at the global, African and national levels have become active in containing the pandemic. The containment measures include capacity building for health workers, management of infected persons, development of guidelines for the management and prevention of the disease, development of tools and materials for diagnosis and treatment, including vaccines. These containment measures, if not properly managed, may divert resources from routine health services and result in declining coverages of immunisation services and outbreaks of vaccine preventable diseases.[1,2,18-20]

Region	Total cases (New cases in last 24 hours)	Total deaths (Deaths in last 24 hours)
Global situation		
Global total	6,194,533 (113,198)	376,320 (4,242)
Africa	108,121 (3,879)	2,700 (62)
Americas	2,905,432 (64,718)	163,248 (1,820)
Eastern Mediterranean	536,148 (16,011)	12,899 (272)
Europe	2,175,941 (16,150)	182,416 (1,824)
South-East Asia	283,845 (11,333)	8,000 (257)
Western Pacific	184,305 (1,107)	7,044 (7)
African regional situation		
Central region	12,167 (3,502)	343 (49)
Eastern region	12,809 (3,905)	349 (88)
Northern region	35,365 (7,259)	1,649 (204)
Southern region	25,285 (7,533)	504 (199)
Western region	29,720 (4,965)	626 (99)
African total	115,346 (27,164)	3,471 (639)

Table 2: Global and African COVID-19 situation. Global statistics as at 1 June 2020 (source: WHO) and African statistics as at 26 May 2020 source: African CDC)[1,2]

IMMUNISATION IN THE CONTEXT OF THE COVIDS-19 PANDEMIC

The high infectivity and rapid spread of the COVID-19 which has necessitated social distancing measures, lockdown with restriction of movements and suspension of non-essential services has negatively impacted on health services including immunisation.[1,2,18,19] Routine immunisation activities have been disrupted due to the COVID-19-related burden on health systems and decreased demand for vaccination as a result of physical distancing requirements for SARS-CoV-2 transmission

control or community reluctance.[18] The limitation of travel and movement as well as closure of offices occasioned by the lockdown as part of the COVID-19 containment measures has affected the availability of supplies for and access to immunisation services. Additionally, the risks of infection of health workers, caregivers and clients have also resulted in the suspensions of and reduced demands for immunisation services. Surveillance activities for vaccine preventable diseases have also been affected.

Unfortunately, while the COVID-19 pandemic rages, vaccine preventable diseases remain a threat and some outbreaks of measles have been experienced. Consequently, while efforts to contain the COVID-19 pandemic should be sustained, immunisation should be recognised as an essential health service and must be sustained despite the challenges posed by the COVID-19 pandemic.

COVID-19 IMMUNISATION RELATED CHALLENGES IN THE AFRICAN REGION

The COVID-19 pandemic has challenged all facets of life including immunisation services. These challenges include those that existed before and have been worsened by the pandemic and those that will be experienced thereafter. It is important to identify and address these challenges to minimise their impacts on immunisation services in the African region. The challenges include lack of implementation of the commitments of the leaders to ensuring that all children are immunised and the diversion of resources for the control of the COVID-19. The resources for immunisation services are likely to be reduced further with limited access to international funds resulting from the economic impact of the pandemic. The lives of children will be threatened with vaccine preventable disease outbreaks.[3-9]

The growing population of African countries has resulted in a large pool of eligible children for immunisation in the region. Consequently, without an increase in resources and commitment, the current efforts will not be enough to sustain the present coverage rates.[6-8]

Health systems especially in resource-limited countries have been overwhelmed from the demand for the provision of COVID-19-related services. Human and material resources have been mobilised for the care of infected persons to the detriment of routine services. Consequently, essential health services such as immunisation have been suspended to address the pandemic.[2,20] To state the obvious, successful immunisation programmes require funding, human and material resources. Unfortunately, in many African countries, immunisation programmes have been sustained by international funds and therefore with the COVID-19 pandemic, these sources of funding are threatened. Funds are required (1) to procure and transport vaccines and related materials such as cold chain equipment, delivery of vaccine services including personal protective equipment required for the protection against COVID-19 and (2) for the operation of service points to increase access to services.[6,11,13,17] A UNICEF spokesperson, Marixie Mercado in a UN newsletter on the impact of flight restrictions and the consequent high cost of travel on access to vaccines and related supplies, noted that "Countries with limited resources will struggle to pay these higher prices, leaving children vulnerable to vaccine-preventable diseases such as measles and polio".[21]

The pandemic has also affected immunisation services in many other ways, including increased demand for resources for its control including the building of the capacity of the overburdened and sometimes infected health workers for its control. There has been a decline in demand for health services, including immunisation services for fear of the spread of COVID-19 during these services. The restriction of movement due to the lockdown sometimes prevents caregivers and health care workers from reaching immunisation sites to receive / deliver services.[28,22] Furthermore, as a result of the evolving nature of the COVID-19 pandemic, many plans concerning immunisation services have been suspended.

RECOMMENDATIONS FOR SUSTAINING AND IMPROVING IMMUNIASATION SERVICES IN THE AFRICAN REGION

Despite the COVID-19 pandemic, vaccine preventable diseases have continued and sometimes, outbreaks have been reported. It is therefore important to sustain immunisation activities even during and after the COVID-19 pandemic. Dr. Seth Berkley of GAVI, the Vaccine Alliance noted that "children missing out now on vaccines must not go their whole lives without protection from disease. The legacy of COVID-19 must not include the global resurgence of other killers like measles and polio." The WHO and UNICEF have warned that "more than 117 million children risk missing out on measles vaccines" because of the COVID-19 pandemic and noted that "delivering all immunisation services, including measles vaccines, is essential to saving lives that would otherwise be lost to vaccine preventable diseases".[21,22] Consequently, African nations must live up to their commitments to provide immunisation services for their children wherever they are found. The following recommendations are hereby being made to sustain immunisation services during and after the COVID-19 pandemic.

African leaders must leverage on the commitments made hitherto, while immunisation coordinators and other stakeholders solicit for the implementation of the services.[3-5] Resources must be made available. There is need for the sustenance of surveillance activities for vaccine preventable diseases. At the national and regional levels, the situation must be reviewed regularly to provide appropriate guidelines to health workers and other stakeholders on immunisation services. Despite travel restrictions adopted as part of the COVID-19 control measures, concessions should be made for the transportation of health care supplies and health workers.[18,20,21] Regional and local centres for disease control have played key roles not only in the COVID-19 pandemic but also in the control of vaccine preventable diseases. However, there is need to sustain these activities and integrate related activities for immunisation and COVID-19 control such as surveillance and service delivery for effective resource utilisation. The leaders at all levels should ensure that their expressed commitments to Universal Health Coverage with respect to immunisation are actualised.[23] Additionally, in line with the recommendations of WHO for sustained delivery of essential services during and after COVID-19, leaders at the national level should adjust governance and coordination mechanisms to support timely action to address and optimise immunization service delivery.[24]

Lack of funds and dependence on donors for immunisation services and the control of vaccine preventable diseases continue to pose significant challenges to the attainment of immunisation targets.[5,6,21] The support by partners for sustained service delivery should continue during and after the COVID 19 pandemic considering the global economic and other impacts of COVID-19. Partners should support the integration of services to optimise resource utilisation. The United Nations agencies, UNICEF and WHO should continue to provide support through the development and updating of

guidelines for sustained programme implementation considering different scenarios.[18] These guidelines should be adopted and adapted for use for programme implementation in African countries bearing in mind the frequent reviews of the guidelines occasioned by the changes in the COVID-19 situation and their local situations. These agencies should sustain their efforts towards sourcing for funds, vaccines and related supplies for sustained immunisation services and the control of vaccine preventable diseases in the continent. These agencies should sustain their support for capacity development for optimal immunisation services in view of the requirement for additional skills to effectively deliver on quality and safe immunisation and vaccine preventable diseases surveillance services during and after the COVID-19 pandemic. Immunisation services also require the commitment of other stakeholders at the community and other levels which should include human and material resource mobilisation in support of immunisation services and surveillance for vaccine preventable diseases.

Health workers play key roles in the delivery of health services including vaccinations, surveillance for vaccine preventable diseases, management of persons affected by disease outbreaks such as the recent COVID-19 pandemic. Unfortunately, some may contract diseases such as the COVID-19 in the line of duty and die. It is therefore important to provide them with safe work environment. Health care delivery services must be well planned to minimise the risks to health workers, their clients and the community. Health workers should be provided with appropriate personal protective equipment to reduce their risks of getting infected with SARS-CoV-2 and other epidemics which may coexist such as Ebola disease. Physical distancing and appropriate hand hygiene should be ensured at immunisation centres during the COVID-19 pandemic. Strategies to ensure that clients spend minimal time at immunisation centres during scheduled appointments, include increasing the number of service points and days and delivery of vaccine services at homes along with COVID-19 related services, should be encouraged.

CONCLUSION

Immunisation is no doubt one of the most cost-effective public health interventions. However, despite global and local commitments to universal immunisation, millions of children have not been reached with life-saving vaccines and have been exposed to the risk of vaccine preventable diseases. African children continue to face significant obstacles to accessing immunisation services which has been worsened by the current global pandemic of COVID-19. The pandemic has resulted in diversion of efforts and resources from essential health services with adverse effects on immunisation coverage and outbreaks of vaccine preventable diseases.

Concerned agencies such as the WHO and UNICEF have drawn the attention of stakeholders at all levels to the need for sustained immunisation services during and after the pandemic. Relevant guidelines and suggestions have been provided to guide country efforts in immunisation service delivery which should be adopted and adapted for implementation based on local contexts.

Through this paper, sustained immunisation service delivery is being solicited. Vaccine preventable disease surveillance activities should be integrated with those of COVID-19. Harnessing and effective utilisation of local and global resources should be ensured such that no African child is left behind, unimmunised or at risk of vaccine preventable diseases.

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JOURNAL WATCH

ACUTE ABDOMEN TEMPORALLY RELATED TO SARS-COV-2 INFECTION

Review completed by Brian Eley, Paediatric Infectious Diseases Unit, Red Cross War Memorial Children's Hospital and the Department of Paediatrics and Child Health, University of Cape Town. Email: brian.eley@uct.ac.za

The featured study described a series of five children with acute abdomen, a newly recognised clinical manifestation temporally related to SARS-CoV-2 infection. In this case series SARS-CoV-2 infection was confirmed by PCR in 2 children and by serology in a further 2 children. All five children presented with haemodynamic instability or developed hypotension during the first few days of hospitalisation, two of the children had skin lesions and only one developed respiratory distress requiring invasive mechanical ventilation. All 5 children experienced a marked inflammatory response. Abdominal imaging was shown to be an important investigation, as it ruled out surgically treatable disease in all five cases, thus preventing unnecessary exploratory laparotomies.[1]

In conclusion, this paper provides the first paediatric description of acute abdomen temporally related to SARS-CoV-2 infection. Following recent descriptions of Kawasaki-like disease or multisystem inflammatory syndrome, this study adds to our knowledge of the evolving relationship between SARS-CoV-2 and the paediatric population.[2-4]

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CONFERENCE & SOCIETY NEWS

19th International Congress on Infectious Diseases was initially moved to September 2020 in Kuala Lumpur, Malaysia. However, this plan was revoked and the conference was put on hold until further notice. For information on when this conference will be held visit the International Society for Infectious Diseases website, http://www.isid.org/icid/

38th Annual Meeting of the European Society for Paediatric Infectious Diseases, ESPID *2020*, will be held as a virual meting from 26 to 29 October 2020. For more information visit the meeting website: https://espidmeeting.org/

12th International Workshop on HIV Pediatrics will be held in San Francisco, USA from 16 to 17 November 2020. For more information visit the conference website, http://www.virology-education.com/event/upcoming/10th-workshop-hiv-pediatrics/

7th African Society for Immunodeficiency (ASID) Congress takes place in Khartoum, Sudan in April 2021. For more information visit the ASID website: http://asid-africa.org/en/

12th World Society for Pediatric Infectious Diseases (WSPID) conference will be held from 1 to 4 December 2021 in Cancun, Mexico. For information on the conference venue and dates visit the Paediatric Infectious Diseases Society website: http://www.pids.org/. AfSPID will once more host a dedicated symposium at this conference.

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