

COMMENTARY

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The impact of COVID-19 pandemic on rabies post-exposure prophylaxis services in Asia

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ABSTRACT

Human rabies is a preventable disease through post-exposure prophylaxis (PEP) in rabies endemic countries where enzootic cycle of dog rabies occurs. The COVID-19 pandemic has induced an unprecedented challenge for under-funded and already stretched health-care systems particularly in low- and middle-income countries, which are unfortunately bearing a huge burden of human rabies. An analysis of hospital-based PEP data in India, Nepal, Sri Lanka, and Thailand, focus group discussion and key informant interview have been carried out to better understand the impact of Covid-19 pandemic in human rabies prophylaxis. It is necessary to better prepare for human rabies prophylaxis in future pandemics based on lesson learnt from current pandemic. The PEP should be categorized as an emergency medical service, and it should be part of the hospital medical emergency. Mass dog vaccination against rabies should be accelerated to reduce the risk of potential bite of roaming dogs and pet dogs in communities. It is a wise decision to invest in cost-effective preparedness, i.e., mass dog vaccination rather than costly response, i.e., human rabies prophylaxis.

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Background

Rabies is one of the oldest infectious diseases present in Asia. Annually, the disease causes an estimated 31,000 human deaths in Asia¹ and annual expenditure of over US\$ 563 million² incurred for direct and indirect costs of post-exposure prophylaxis (PEP) in humans and dog rabies control efforts. According to data published by the World Health Organization (WHO), India accounts for 59.9% of deaths due to rabies in Asia, and 35% of deaths globally.³

Dog bites are the primary source of human infection in all rabies endemic countries and account for 96% of rabies cases in the southeast Asia region.⁴ Human rabies is a preventable disease through post-exposure rabies prophylaxis in rabies endemic countries where enzootic cycle of dog rabies occurs. There are issues related to availability, accessibility, and affordability of human rabies vaccines and immunobiological products in normal situation and many people are dying due to rabies. Post-exposure rabies prophylaxis is the last resort for prevention of human rabies even when people are exposed to rabies virus through animal bites. The situation will remain same unless rabies is controlled at source using One Health approach, i.e., interrupt the enzootic cycle of dog rabies through mass dog vaccination and dog population management.

The impact of the COVID-19 pandemic on essential health services is a matter of great concern. Major health gains achieved over the past decades can be wiped out in a short

period of time. The operation of health services may be affected by shifting resources to fight the COVID-19 pandemic or by closure of health services or facilities.⁵ The sudden outbreak of Covid-19 pandemic has disrupted vaccine supply and prevented dog bite victims to seek PEP due to travel restriction, lockdown and closing of urban centric anti-rabies clinics. The COVID-19 pandemic has induced an unprecedented challenge for under-funded and already stretched health-care systems particularly in low- and middle-income countries (LMICs), which are unfortunately bearing a huge burden of human rabies.

Materials and methods

Analysis of hospital-based PEP data in India, Nepal, Sri Lanka, and Thailand, focus group discussion and key informant interview were used to gather data and information for impact assessment of Covid-19 pandemic in rabies PEP in Asian countries. The hospitals selected in above-mentioned countries are major anti-rabies clinics in those countries. An attempt has been made to document lessons learnt from Covid-19 pandemic in human rabies prophylaxis based on discussion with frontline workers in rabies endemic countries so that we can better prepare for human rabies prophylaxis in future pandemics and also sustain what has been achieved so far for prevention of human rabies in new normal situation.

Results

Health-care services for rabies prevention

The WHO conducted the Pulse survey on continuity of essential health services during the COVID-19 pandemic. The rapid assessment survey results showed that disruptions of essential health services were reported more in lower-income countries. Seventy-six per cent of countries reported reductions in outpatient care attendance owing to lockdown, staff redeployment to provide COVID-19 relief, unavailability of services owing to closures of health facilities or health services, and supply-chain difficulties.⁵ The emergency services were the least disrupted, although 16 countries reported disruptions across all emergency services. It should be noted that weak surveillance in rabies-endemic countries makes assessing the pandemic impacts challenging.⁶ The disruption of health services is particularly problematic for those living under poverty. Many dog-bite victims did not visit public hospitals as they fear contracting Covid-19, or they were not sure whether they were operational for PEP services.

Most rabies endemic countries in Asia have been practicing cost-effective intradermal (ID) rabies vaccination promoted by WHO but it may be a challenging task to continue ID schedule due to limited number of patients seeking PEP and intramuscular schedule has to be introduced. The patients and staff at the animal bite treatment centers needed to follow strict safety protocols to continue their life-saving efforts against rabies.⁷

Rabies incidence

It is difficult to understand magnitude of rabies incidence in the context of Covid-19 pandemic when number of people seeking PEP was reduced by 37% to 71% in 2020 (except Sri Lanka) when 2019 was considered as base year as shown in Table 1.

Medical staffs from most hospitals providing PEP services were repurposed for Covid-19 pandemic response as it was an unprecedented global public health crisis. Dog bite incidence may be low as travel restrictions and lockdown were imposed. As a result, people did not come out of their houses, children remained at home due to school closure and chances for dog bite exposure may be comparatively low. Unlike other infectious diseases, telemedicine is not a solution in case of rabies as it requires specific vaccines and immunobiological products which are available in designated anti-rabies clinics and dog-bite victims have difficulties to reach these clinics due to travel restriction and uncertainty of logistic issues such as transport, vaccine availability etc. It was a big surprise in Sri Lanka where most of the peripheral anti-rabies clinics were unable to function due to Covid-19 pandemic and they referred patients to

designated hospital for PEP as seen in National Hospital Colombo. It is also justified by availability of 24/7 PEP service for dog-bite victims in emergency unit of designated hospital free of charge. On the other hand, routine dog rabies vaccination campaigns may have been suspended due to travel restriction, logistic difficulties, and lack of interest in the community to vaccinate dogs due to Covid-19 fear. The rabies surveillance activities were also suspended or suffered from chronic problem of gross under reporting.

Logistics

The increased public sector investments for human rabies prophylaxis including free PEP service, as well as programs to eliminate human rabies as a public health problem are favoring growth of the market of rabies vaccine and immunobiological products in Asian countries. The market in Asia is expected to witness significant growth owing to active involvement by manufacturers in Asian countries such as China and India regarding development of innovative rabies vaccine and passive immunization products. The number of dog bite victims seeking PEP is expected to increase in proportion to urban population as it is available free of charge in public hospitals and clinical practitioners will not take risk unless rabies free areas are declared, where dog-mediated rabies exists. Since public is historically aware that rabies is 100% fatal disease, dog-bite victims often ask for PEP after consulting a medical doctor.

There was a disruption in supply and availability of human rabies vaccine and rabies immunoglobulin (RIG) in the international market. It was difficult to manage regular supply of human rabies vaccine due to lockdown and closing down of borders by many countries in the wake of Covid-19 pandemic. Indonesia has licensed only one human rabies immunoglobulin (hRIG) supplier which raised price by ten times owing to international shortage of hRIGs and they requested WHO to arrange emergency supply of hRIG and agreed to permit supply of hRIG from other sources which offered reasonable price for hRIG which has a longer shelf-life. The public sector has been responsible for supply of human rabies vaccine and RIGs, but they have to follow government procurement procedure which was hampered by restrictive conditions imposed by Covid-19 pandemic in production, marketing, transportation and distribution of vaccines and RIGs.

Discussion

The pulse survey provided insights from key informants from countries on the extent of disruptions to their health services during Covid-19 pandemic and an indication of their experiences in adapting strategies to mitigate the impact on service provision.⁵ The COVID-19 pandemic has demonstrated possible disruption of PEP services in rabies endemic countries which may result in unprecedented increase in incidence of human rabies. It is reasonable to anticipate that even a modest disruption in essential health services could lead to an increase in morbidity and mortality from causes other than COVID-19 in the short to medium and long term.⁵

Table 1. Hospital-wise percentage of PEP in 2020 as compared to 2019.

Anti-rabies clinic	Country	% of PEP
Queen Saovabha Memorial Institute Bangkok	Thailand	52.3%
Institute of Preventive Medicine Hyderabad	India	71.1%
Safdarjung Hospital, New Delhi	India	36.6%
Sukraraj Tropical & Infectious Disease Hospital Kathmandu	Nepal	61.3%
National Hospital, Colombo	Sri Lanka	115%

The COVID-19 pandemic is a wake-up call as similar epidemic/pandemic events may occur in future. The available data showed that progress in preventing and controlling rabies at source, i.e., dog rabies, has been inadequate, under-funded and deprioritized in LMICs. It is understandable as animal health sector has to focus on economically important livestock and poultry diseases and many of them are of transboundary nature. Rabies is considered mainly public health issue and Ministry of Health spends huge fund for human rabies prophylaxis although public investment in mass dog vaccination is cost-effective, logical, and sustainable to prevent human rabies. The Department of Health (DOH), Philippines set an example of providing dog rabies vaccine to animal health authority to accelerate mass dog vaccination campaign as it was an investment for human rabies prevention. The DOH believes that one of the most viable strategies to curb the alarmingly high rabies cases in animals and humans is still massive dog vaccination.⁸ There is no end game of rabies unless animal health sector recognizes their contribution in prevention of human rabies through dog rabies control and subsequent elimination. Those rabies endemic countries which have institutionalized mass dog vaccination and dog population management as an integral part of the national rabies elimination programme were in better position to observe negligible number of human rabies cases despite disruption of PEP services. On the other hand, those countries already practicing cost-effective ID rabies vaccination were efficiently managing vaccine demand despite supply chain difficulties. Thailand is a classic example. Thailand has pioneered cost-effective ID rabies vaccination technique which helped national authority to manage vaccine supply in efficient way and mass dog vaccination has been accelerated in recent years. As a result, the number of positive animal rabies specimens in Thailand had decreased from 1,724, 343 and 168 in 2018, 2019 and 2020 respectively. The decline of positive animal rabies cases during COVID-19 pandemic might partially be related to poor accessibility to animal rabies diagnostic services but it is the fact that annual number of reported human rabies cases in Thailand is below five in last 3 years.^{9,10}

One of the major challenges of Covid-19 pandemic communication was misinformation or disinformation about vaccine and treatment. It is interesting to observe in Sri Lanka that Covid-19 vaccine was not given to those who were receiving anti-rabies vaccine as vaccinator was hesitant to enroll them in Covid-19 vaccination programme. There is no contraindication to give Covid-19 vaccine to those patients who were receiving anti-rabies vaccine and such rumor or misinformation must be denied by nodal agencies.

Some countries have been facing difficulties in procuring hRIG or equine rabies immunoglobulin (eRIG) during pandemic partly due to complex and limitation of production system compounded by lack of demand forecast, disruption of international air transport chain and tedious public procurement procedure. Several countries reduced human rabies vaccine procurement in 2020 and forecast reduced procurement in 2021 and beyond.⁶ On top of that, some countries have licensed one or two RIGs available in international markets and there is no WHO pre-qualification system for eRIG and hRIG. As a result, it was impossible to make available

emergency medical product due to short supply, high price quote complicating standard procurement process. However, it was easier in countries where RIGs have been classified under essential drug list which helped hospital administrations for emergency procurement of RIGs. The chronic global shortage of RIGs and production limitation have led to the development of alternative immunobiological products. The transition from RIG to rabies monoclonal antibody (RmAb) has been strongly recommended by the WHO with the aim of achieving an adequate supply, a reduction in the production costs, a reduction in adverse reaction risks, and the availability of consistently active batches.¹¹ In addition, monoclonal antibodies come in the form of a concentrated product, they can be more useful than RIG at wound infiltration which is in line with new WHO recommendation for passive immunization.¹ Currently two RmAbs are available in Asian markets which are expected to replace hRIG and eRIG in coming days as there are limiting factors for production and use of conventional RIGs. National authorities should create an enabling environment (education, inclusion in essential medicine list, regular supply) for use of RmAb for passive immunization in national PEP guidelines as recommended by WHO.¹²

There is a need of paradigm shift in strategic approach for rabies elimination, i.e., prioritizing and investing more in mass dog vaccination rather than animal birth control and PEP which will be cost-effective and sustainable in achieving global target of zero human rabies death. Pool funding of a comprehensive rabies elimination programme with a focus on mass dog vaccination supported by a robust surveillance of animal rabies will be critical to accelerate rabies elimination drive in LMICs. It is evident that rabies transmission to humans can only be curtailed if we have above 70% of dog vaccination coverage to break dog-to-dog rabies transmission in Covid-19 pandemic like scenario. Since rabies virus does not recognize political boundaries and presence of rabies in any country or territory, regionally coordinated rabies elimination campaign is a must to garner collective political commitment and to accelerate zero human death by 2030.

Conclusion

The Covid-19 pandemic response has shown that we need whole of the government and whole of the society approaches to deal with unprecedented pandemic situation and repurposing of health staffs and budgetary provision is expected and justifiable. It is not possible to continue business-as-usual approach under pandemic and a contingency planning should be developed based on lesson learnt from Covid-19 pandemic response. There was policy, administrative and logistic challenges for continuation of human rabies prophylaxis in the pandemic situation. Minimum support staffs for PEP services need to be identified, hotline consultation service needs to be established for public communication and response, emergency supply of vaccine and immunobiological needs to be ensured through policy and administrative decision for protracted events. The PEP should be categorized as an emergency medical service, and it should be part of the hospital medical emergency to ensure that dog bite victims may have access to PEP when anti-rabies clinic is closed beyond office hour.

Mass dog vaccination against rabies should be accelerated to reduce the risk of potential bite of roaming dogs and pet dogs in communities as future pandemic may be expected sooner or later. In other words, it is a wise decision to invest in cost-effective preparedness, i.e., mass dog vaccination rather than costly response, i. e. human rabies prophylaxis. Pool funding of dog-mediated human rabies elimination programme is an innovative One Health approach for meaningful engagement of animal health sector in achieving zero human death by 2030.

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