

Of Late is the 'Covid-19' Among the Re-Emerged Viral Infections during Recent Years and what next? Possible Reasons and Precautions

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Received date: June 29, 2022, Manuscript No. IPMCRS-21-10550; **Editor Assigned date:** July 01, 2022, PreQC No. IPMCRS-21-10550 (PQ); **Reviewed date:** July 13, 2022, QC No. IPMCRS-21-10550; **Revised date:** July 22, 2022, Manuscript No. IPMCRS-21-10550(R); **Published date:** July 29, 2022, DOI: 10.36648/2471-8041.8.7.237.

Citation: Venkataramana M (2022) Of Late is the 'Covid-19' Among the Re-Emerged Viral Infections during Recent Years and what next? Possible Reasons and Precautions. Med Case Rep Vol.8 No.7: 237.

Abstract

Viral infections often created the significant threat of severe illnesses and death worldwide. This situation is more apparent in under developed and developing countries. There are four major genomes (double stranded DNA; single stranded DNA; double stranded RNA and single stranded RNA) that usually viruses possess. The virus diseases which ravaged the world during the late 20th and early 21st centuries are RNA viruses. The viruses with RNA as their genome show uniqueness in multiplication and adaptation characteristics. The replicase of these viruses has the less proof-reading activity and prone for frequent mutations which help them to adapt positively. Dramatic climate change has witnessed for the past 30 years due to which the RNA viruses might force to attain genetic mutations for their survival and hence lead for the increased virulence. This situation may worsen in future and hence proper precautionary measures with at most care is required to handle the newly emerging pathogenic viruses

Analysis

At least ten different viral infections [COVID-19 (SARS-2), Nipah (NiV), Ebola, Swine flu (H1N1), Zika, Middle East Respiratory Syndrome (MERS), Severe Acute Respiratory Syndrome-1 (SARS-1), Dengue (DENV), Chikungunya (CHIKV) and Human Immunodeficiency Virus (HIV)] caused significant morbidity and mortality and created panic across the globe during recent years. These disturbances peaked from the beginning of the 21st century irrespective of the time of origin of the above viruses. Interestingly all the above listed viruses are enveloped of which the genome is the same ie the single stranded RNA (Table.1).

The RNA viruses are known to be easily vulnerable for external pressures and attain mutations in their genomes in order to fit into the changed environment for their multiplication and survival [1]. In addition, the enveloped viruses are highly unstable compared to the naked. The replicase of these viruses has the less proof-reading activity and facilitates these unstable viruses to undergo frequent mutations which may help them to adapt positively.

S.NO	Virus Name	Family Name	Type of genome	Envelop	Year of origin	Year epidemic caused	of
1	SARS-2(Covid-19)	Corona viridae	RNA	Yes	1960	2020	
2	Zika virus	Flaviviridae	RNA	Yes	1947	2018	
3	Nipah Virus	Parainfluenza viridae	RNA	Yes	1999	2017	
4	Ebolavirus	Filoviridae	RNA	Yes	1976	2017	
5	Dengue virus	Flaviviridae	RNA	Yes	1907	2005-15	
6	MERS-CoV	Corona viridae	RNA	Yes	1960	2013	
7	Swine flu Virus	Influenza	RNA	Yes	1918	2009	

8	Chikungunya virus	Togaviridae	RNA	Yes	1952	2005
9	SARS-1	Corona viridae	RNA	Yes	1960	2003
10	HIV	Retroviridae	RNA	Yes	1920	1987

Table1: Certain viruses that caused significant morbidity and mortality across the world.

Many of the above viruses were discovered at least 50 years back but their disease causing potentiality in terms of virulence is increased drastically only from the late 20 and early 21st centuries. The above change can be noticed in terms of the research articles published on the respective virus infections (Figure 1). Several lines of research on different viruses are being tried to address the genetic difference between the mild and severe virulent strains. Apart from that, it is also equally important matter of concern to analyse the force that drives the viruses to undergo genomic mutations and sometimes makes them to evolve as high virulent strains. HIV occupied the top of the list of viral infections in terms of mortality and panic created in the society. Perhaps it may be also on the top with reference to the budget allocation for the research. However, it is well known fact that the development of vaccine or the potential drug is being hurdled until now due to the hyper genetic changes in the HIV genome being attained time to time [2]. Likewise, in case of dengue virus also, the documents showed that the severe forms of the diseases Dengue Haemorrhagic Fever (DHF) and Dengue Shock Syndrome (DSS) have been increased unlike the situation that the dengue was considered to be as self-limiting. Until 1970s only few countries were reported of dengue infections with only serotypes 1 and 2 but by the year 2000 more than 125 countries were added in the list of which several countries were noted with hyper-endemic infections with all four serotypes [3]. Further, the dengue virus serotype 4 seems to be evolved drastically during recent times [4].

with severe illness noticed during 2005 in many countries across the world [5]. This development supports the possible changes in CHKV genome which would support the better adaptation and vigorous multiplication and hence lead to the severe disease. The origin history of zika virus stems in the year 1947 which belongs to the virus family Flaviviridae that dengue virus also belongs. The symptom expression shows the commonality with dengue and chikungunya viruses. All these three viruses transmit by the same mosquito species *i.e.* *Aedes aegypti*. Zika virus is reported to be evolved in 20th century and attained adaptive mutations in nature [6]. Eventually world witnessed the remarkable effect of zika virus in terms of morbidity and mortality especially with reference to the infants. Interesting fact about the dengue, chikungunya and zika viruses is that their involvement in co-infections in a single patient [7, 8]. These developments were recorded only in 21st century although their origin took place long ago which explains that these viruses might attained the genetic changes which would help them in causing increased number epidemics, co-circulation and hence got the opportunity to cause the co-infections. More research may be required to decipher the outcome of such co-infections. The viruses like NiV, Ebola, and SARS-1, were nowhere before the year 2000 although their identities were recorded way back (Table. 1).

Nipah virus emerged recently and caused mysterious symptoms before killing the infected [9]. This virus has evolved to cause such a dreadful disease in 21st century although the virus had chosen the human as host 100 years ago. In this case, it is important to notice that none of the other viruses created that much panic situation that forced to the removal of the deceased without an opportunity for the nearer/dearer to have a final look. The out breaks of ebola created ravaged situation in the affected countries due to its potentiality in causing the disease to the greater number of people and high percent mortality during the recent years [10]. Swine flu is known to be attaining genetic changes by two processes, genetic 'drift' and 'shift', during different time periods and recorded epidemics. This virus causes symptoms similar to the seasonal common cold and eventually turns into severe disease in few cases, finally ends with death. The 2009 swine flu virus which caused the outbreaks in many countries is the resulted combination of genes re-assorted from the strains of pigs, avian and humans (11).

The corona viruses viz SARS-1, MERS and SARS-2 (Covid-19) tops list of viruses causing severe respiratory infections (adeno, influenza and para influenza, respiratory syncytial virus, picorna viruses etc). Covid-19 which has been reported in the year 2019 reached to the world pandemic at the fastest rate in the history

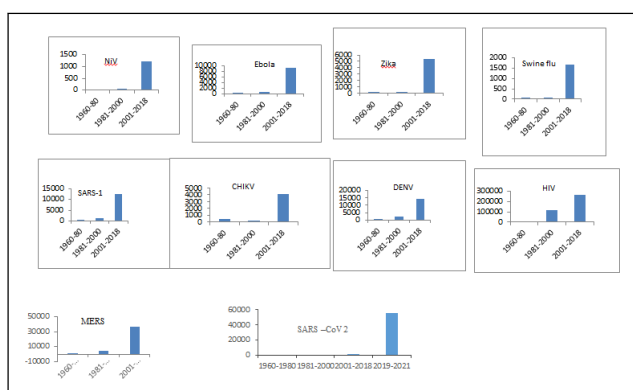


Figure 1: Bar diagrammatic representation of number articles published for the viruses [(NiV), (Ebola), (Swine flu), (Zika), (SARS-1), (DENV),(CHIKV), (HIV), (MERS) (Covid-19)] during the periods 1960-80, 1981-2000 and 2001-present.

The above developments are due to the evolution of DENV into many genotypes with genetic mutations time to time. The first report of CHKV happened during 1945 but the outbreaks

of human virus epidemics. This virus infections spread to more 220 countries infecting nearly 203 million people with death toll of 4.3 million. The devastation still continuing. Few unique characteristics of this virus aided in the fast spreading and the severe illness. In general, the genome size of the DNA viruses will be larger (100-200 kb) and hence some part of the genome will be dedicated to evade the host immune system. The genome size of the RNA viruses will be lesser (7-12 kb) but these viruses evade the immune system by undergoing frequent mutations. In this context, the genome size of the coronaviruses is larger (~ 30 kb). Hence these viruses applies two mechanisms in the process of avading the host immune system which is advantage for virus in fast spreading and in causing severe illness. The two mechanisms are 1. the ability to dedicate some portion and 2. Undergo mutations (being a RNA virus). In addition, the ligand (spike)-receptor (ACE2) interaction is appears to be irreversible (in case of many viruses this step is reversible) in case Covid-19 virus and hence leads to the nearly 100% infection in exposed cases (Figure 2). These unique features gained by the Covid-19 are due to the genetic mutations and the additional mutations are already posing for the increased threat.

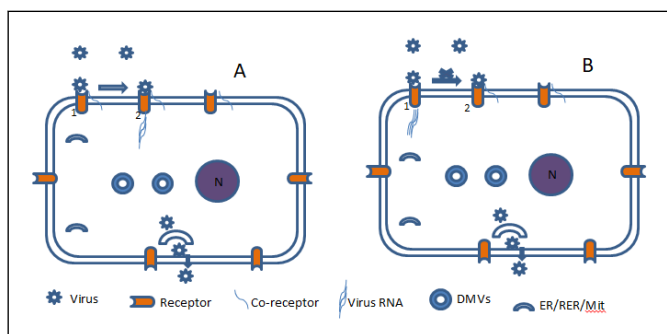


Figure 2: Diagrammatic representation of the life cycle of A) an RNA virus and B) SARS Covid-19. It appears that the Covid-19 attach to the host cell receptor irreversibly (in all other viruses, the initial attachment stages will be reversible). This step may increase the efficiency of the virus infections.

One of the facts to be considered is the drastic change of climate for the past few decades which might force the above viruses to attain the frequent and fast genetic changes. Dramatic climate change has witnessed for the past 30 years due to which the viruses might force to attain genetic mutations for their survival and hence lead for the increased virulence. The global environmental scenario indicates that this situation may worsen in future and hence proper precautionary measures with at most care is required to handle the above listed or newly emerging pathogens. Over the past few years, the global temperature has been increased/decreased to various extents in different countries [11]. Majority of the above listed viruses have originated and evolved from the African continent which records high temperatures throughout the year. The climate change influenced the environment in such a way that it leads to either severe drought or flooded rains during unusual timings. It has been also witnessed the tsunamis, earthquakes and the volcanoes. In addition to the above, increased pollution has been noticed in some geographical areas. It was predicted that the climate change or the natural calamities may force the virus

vectors to migrate to different geographical areas and involved in spreading the viruses into new locations [12]. The new environmental conditions may force the viruses to undergo adaptive mutations or the viruses may get the opportunity to exchange to genetic material with the existing viruses. Such instances lead for the origin of new strains. The above natural calamities were recorded mainly in the countries like India, Malaysia, Indonesia, Thailand, Nepal, USA, Brazil, Philippines, Japan etc. Incidentally, the above listed viruses either re-emerged or caused epidemics in the above countries during recent times.

Hence, the possibility of influence of climate/pollution on the viruses, like COVID-19, NiV, Ebola, Swine flu, Zika, SARS, Dengue, Chikungunya and HIV having the RNA as their genome cannot be ruled out, of undergoing gene mutations and turned into high virulent and severe disease causative agents. In addition, there are very high chances of repetition of viral epidemics or pandemics in the future also with re-emerging virus strains or the newly emerging viruses and hence careful precautionary measures are required.

Suggested Precautions

While attempting to understand the reasons for virulence of the viruses, there is a need for formulating control or precautionary measures. Although the environmental protection is the best choice but has huge limitations as it depends on several factors in different countries. Designing and development of drugs or vaccines is being continuously attempted for the listed viruses. But the fact to be accepted is that none or very few are crossing the pre-clinical stage and not reaching to the stage of public use. Hence the alternative is to formulate the precautionary measures. Considering the characteristics of the above listed viruses or possible new emerging viruses, the suggested precautions would be

1. Bringing wide awareness about the past or ongoing virus epidemics across the society.
2. Research for developing specific and fast diagnostics, therapeutics and vaccines.
3. Continuous monitoring for the re-emerging or newly emerging virus infections in suspected regions or the countries.
4. Establishing diagnostic centers at the international air ports.
5. Controlling of the breeding of transmitting vectors.

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