ISSN No:-2456-2165

Battle between Human and Viruses: An Antidisease Visual Approach on Viruses' Aduptive Nature to Concentrate as an *Endurance Endeavors*

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Abstract:- Humans were battling for survival before evolution till our modern lifestyle. Amongst all, viruses are such tiny organisms keep infecting a humans a decades ago and spreading in universe by many routes/pathways. Animal to human transmission is triggered outbreaks claiming thousands of lives, in a period of time by different species of viruses. RNA genome viruses are assumed to more virulent than DNA genome one due to its complex structural instability , environmental adoptability, mutational properties. Study of its entry in human body, attachment and replication into host cells, response of host defence cells by innate and adaptive immunity is helpful to know virus' mild to lethal pathogenic nature. Marburg, Ebola, HIV,influenza, SARS-COV, and 2019 –nCoV(COVID 19 /SARS-COV2) are few deadly threats of a battle. Study by lab investigation, vaccines, antiviral drugs need to focus on antidisease approach then anti pathology visionary to eradicate and protect human from viruses' bioweapon use.

Keywords:- *Viruses, immunity , 2019-n COVID, antidisease approach.*

I. INRRODUCTION

Virus is a teentsy pathogen, exists as an independent particle found in every echo system .Its structural genetic material is a molecules of either DNA or RNA, encodes 4 proteins in a simple to 100-200 proteins in a complex form.

Virion, an entire virus particle contains nucleic acid may be single or double stranded enclosed within protein coat/ capsid .Though less DNA and RNA material with limited number of genes, virus encodes all genetic information to form large capsid through this nucleic acid ,so named nucleocapsid . Outer core is called lipid envelop.

Shapes of viruses vary from simple helicle (TMV-tobacco mosaic virus) , icosahedral form to more complex structures. It is a contagious, replicate solely inside the living cells of the either animals and plants and disperse sequence of genomes by multiplication and mutation .

Marburg, Ebola, Rabies , HIV,Herpes simplex, Smallpox, Hanta, influenza, Dengue, Rota, SARS-CoV -2(2019-nCoV) are few deadliest viruses had put nature and lives in danger through endemic, epidemic or pandemic spread. Pathogenicity and existance of each one are depend on their diverse aduptive ecology/nature with different environs. Cure of infection , possible immunization at community level and / or global eradication are a challenge for medical profession which necessitate to explore virus with time.

II. DISCUSSION

- *MARBURG VIRUS:*

Marburg virus is a filamentous negative sense, non segmented RNA virus from filoviridae family which encodes seven genes.[1] It was first found in1967, germany, continued outbreak till 2017 uganda, with 4th number of infection with upto 90% fatality.[2] Virus infected bats infects humans through abraded skin and mucosa, low aerosol transmission and fatal parenteral exposure.[3] Incubation period 2-21days. Accurate disease progression begins with flu-like symptoms chills, sore throat, headache, painful muscles and joints, alveolar congestion. Other symptoms include bleeding from mucosa, fever, bloody vomitus and watery diarrhea.[3] Diffuse skin rashes with petechiae initially and aggressiveness , seizures and coma in later stage. Mild to severe necrosis in spleen ,liver ,kidney and lymphoid tissue depletion by apoptosis without viral antigen [2] Death due to irregular immune response , dehydration and haemorrhage with intravascular coagulation and survival sequels visible with arthitis, conjunctivitis , pschycological upset. Social separation is helpful for recovery. [3] It was programmed as biological weapon during cold war for offense and defence.

- *EBOLA VIRUS:*

Ebola virus is same as Marburg virus in structure, negative-sense, single-stranded RNA viruses of ebolavirus genome and Filoviridae family, with highly infectious nature. It was first recognized near the Ebola River valley during in Zaire in 1976with current outbreak in 2018-19 with epidemiological data of 40 years [4 ,5] **H**uman transmission of Infection occurs through close contact with infected animals' body fluids.[5] It also shows 50-90% lethality due to hemorrhagic symptoms by endothelial cell toxicity and hypovolemic shocks.[4,5] Infection course is 14-

21days.[4] Virus matrix protein provides important insights for its replication and rapid progressive pathogenesis. Knowledge of innate immunity requires study about production secreted glycoprotein antibody after infection (sGP) which is not produced by MARV. Infection is visualized in early and preferred targated cells, Monocytes (dendritic cells (DCs)) and macrophages by ebola virus.[5, 6] Virus evades immune responses like that in HIV5 and herpes virus [4]

➢ *RABIES VIRUS: (RABV)*

Rabies virus is rabere (to be made in latin), bullet shaped enveloped virion, negative sense single stranded RNA genome [7], It is a zoonotic virus that of genus Lyssavirus of Rhabdoviridae family and of neuroinvasive nature. It was first found in Babylon monkey in the 2300 BC in Egypt .Louis Pasteur had identified in 1880 with first vaccine immunization applied in 1885'. It is fatal, progressive, 7th grade endemic infection of nervous tissue affecting all warm-blooded animals, with panic health issue in asians and Africans. Amongst multiple genotypes most are causing human infection. Transmission through rabid animal bite at peripheral site and gained entry of infected saliva through open, abraded skin wounds, Raba particle inhalation ,organ and cornea transplants. Bites with bleeding are of acute onset and most risky.[10] More than 60000 deaths per year are counted worldwide. RABV eclipse phase is 2 weeks to 6 years.[10] Retrograde axonal centrifugal spread occurs along with PNS path in ascending manner from CNS after invasion of CNS from peripheral site of virus uptake into body. [8] 10 days after virus gain entry into human body, itching , pain and paresthesia are present at the bite wound site. Neuronal dysfunction, [9] cell to cell spread, [8] N2o induced toxicity are present. Negri bodies, neurovirulence [8] but no neuron apoptosis and inversely related pathogenicity to virus replication are definite characteristics of RV. Symptoms include degeneration of ganglion cells, salivary, adrenal and lacrimal glands, thrombosis and haemorrhages in vascular system and, generalised flaccid paralysis. Preventive and post exposure immunization by injectable live or dead viruses with protocol of 0,7,28 days and booster dose every year is recommended for control of rabies endemically.

➢ *HIV VIRUS:*

HIV virus is a retro virus of Lentivirus [13] family with long letancy ,[13] persistent replication and CNS involvement.[11] HIV -1 And HIV -2 are the viral antigen types . RNA genome Of HIV-1 is 2 single stranded molecules enclosed in protein core and lipid membrane It cannot survive outside the bloodstream or lymphatic tissue and easily inactivated by the exposure to common detergents and disinfectants.[13]. Virus was first introduced in humans through African chimpanzees in1920-1940. Virus enters into body through mucous membranes, injured skin or mucosa and by parenteral path. HIV can be transmitted through blood,plasma or serum organ transplantion and artificial insemination. All CD4-positive cells 13(permanent reservoir of virus)such as , dendritic cells ,T helper cells, macrophages[13] and astrocytes are susceptible to HIV. Assumption of incubation period is several weeks at4*c. Sexually transmitted virus attaches first to dendritic cells (e.g. Langerhans cells) or macrophages[12] then reach to Blood monocytes, where it replicates. From day one to 14 days period, HIV is detected in lymphoid tissue , lymphnodes, whole body with nervous system involvement .HIV 2 pathogenicity is lower than HIV 1. HIV -1 infection course is pandemic. [11] Frequent period of illness increases with its course of infection includes mild fever, diarrhoea , fatigue, weight loss, opportunistic infections[13], neoplasms[13] , impaired neuronal and cerebral functions ,oral and skin infections highlighten generalized immunodeficiency. [13] ELISA and Western blot test, NAT assay provides confirmatory investigation . Infection course is chronic and fatal as trial of vaccine since 1983 is unsuccessful so no eradication virus is possible till date. [11] Reduction of HIV infection through blood and plasma donor is possible after 2004 with safe and quarantine collections.

➢ *HERPES SIMPLEX VIRUS (HSV):*

HSV is a neurotropic double-stranded DNA virus which belongs to Alphaherpesvirinae (Herpesviridae) family[15]. Herpes means to creep/crawl [17] as cold sore, described in Rome (AD100) as blister on ladies' lips.[18] Herpes was found near 1940s . Orolabial infection in the late 19th century with 2 types identification near 1960's. Amongst two types [14,18] HSV1 is more common causes mouth, throat, face, eye, and CNS infections, whereas HSV-2[15] causes primarily anogenital infections.[17] Both are unique biologically in neurovirulance, latency and reactivation of infection. Close contacts at virus shedding[14] secretory surface of infected one plays a role for virus transmission eg. Perinatal infection at the time of child birth.[14] Virus is inactivated at room temperature and by drying, so no aerosol or fomite spread of virus is [17,18] **Virus** enters through abraded skin or mucous membrane[14] replicates in the ganglion cells. Primary infection starts within five days of short incubation period, inoculate in ganglions. Centrifugal migration spread of virions to mucosal skins through trigeminal [18] and other ganglions by sensory and motor nerve infection. Initial crop of vesicles visualized with the large surface area with recovery from neural tissue. Due to contagious nature, virus spreads via autoinoculation at distance from neurons innervating via inoculation. virus allows disease extension. Ganglion are the reservoirs of viruses due to lifelong latency of virus[14,15,16] HSV infection causes orofacial and genital herpes[14], herpetic whitlow, herpes keratitis and encephalitis[14], knife cut erosion in skin , herpetic sycosis is infection hair follicles , eczema herpeticum , multiple, round, superficial oral ulcers[18] accompanied by acute gingivitis. Neonatal herpes is morbid and fatal. Recurrent outbreaks are common amongst the immunosuppressed persons. Prevention by use of condomand antiviral drugs.281

➢ *SMALLPOX (Variola):*

Human existence of variola virus since1763,orthopox genus[20,21] contagious[19], double stranded DNA virus[19,22] structured with core ,lateral body, membrane and envelop. Virus spreads in human to human contacts[19]by air born

droplets. Variola major[20] affects 90% and variola minor affects only 2%[19]in previously vaccinated ones.. Smallpox virus is resistant to environmental changes.[21] Its a infection of skin[20] (squamous epithelium)and mucous membrane%, oropharynx. [20] It is completely eradicated by 1980 (WHO) with vaccines. Belief of use of massive endemic virus as bioterrorist weapons[19,20] was programmed for invading ohio river velly by the English[19]. Pathogenicity visualized after direct contact, body fluid and aerosol inhalation from infected person. Symptoms appear within 7–17 days˜ after exposure with high fever, spike for 3-5days , myalgia, and headache. A maculopapular rashes [22] erupt on the face and neck, convert as papules become round and firm vesicle **within dermis and** measure 2–5 mm in diameter.Lethal variant[22] flat small pox' in children was without pustule ,vesicle and skin eruption, [20] After 9-10 days of exposure crusting and scabs[20,22] will appear **.** Pitting scars [21,22] appear after infection resolution.. Death may occur due to toxaemia , pneumonia.[19] Morbidity as pockmarks**[19,20,22]** are found in upto 80% and blindness due to viral keratitis[19] upto 1% of in virally infected survivors. Arthritis , encephalitis resulting in either retardation or death of a person is rare. Patients' isolation and moniterization for fever~, swab sample reports, PCR assay%, health supportive measures and successful ring vaccination chain has proven helpful for virus eradication from the world in1977**.** [19]

➢ *HANTA VIRUS:*

Hanta virus is round, pleomorphic or tubular particle *of Hantavirus* genus within the family of *Bunyaviridae of* three-part segmented negative-sense, single stranded RNA genomes*. Disease named as Virus-induced haemorrhagic fever with renal syndrome (HFRS) are found in Russia as early as 1913; Human/ Huntavirus pulmonary syndrome (HPS) in 1993 named by Hughes et al., 1993and as hantavirus cardiopulmonary syndrome (HCPS) (Hallin et al., 1996) as of today. [23,24] Hantaan virus (HTNV), was identified in 1978 by Lee *et al*. near small river called Hantaan. Until now, 21 species and more than 30 genotypes can be found in the world [23] Virus is transmitted in humans by excreta of rodents and insectivores, arthropods when becomes airborne, rodent bites and blood transfusion.. Humans are dead end host for this virus.[24] Entry into cell facilitated only by fusion with endosomes**.**[25] Global estimation by Jonsson et al in 2010,that aproximately1,50000 people get infected per year [23,25] by fatal hemorrhagic fever with renal syndrome (HFRS), clinical symptoms include fever, renal dysfunction, haemorrhage / leakage due to increase microvascular permeability and shock. Hantavirus cardiopulmonary syndrome (HCPS) is with added symptoms of gastrointestinal tract followed by non-cardiogenic pulmonary oedema, leads to shock [26] The clinical course is subdivided into five phases: Febrile, hypotensive, oliguric, diuretic, and convalescent. Phoptophobia, conjuctival bleeding, petechiae, hematuria , proteinuria, hypotension and shock, and at last upto renal failure within 3wk to 6 month .vaccination is not successful .innate immunity is developed after infection. No antiviral drug can be effective, only give supportive therapeutic measures**.**

➢ *INFLUENZA VIRUS :*

Influenza virus, human respitatory virus,possess RNA genome of *Orthomyxoviridae family*. Influenza A viruses (IAV), influenza B (periodically epidemic) viruses are virulent to humans and influenza C(endemic and mild) . Virus causes seasonal with annual winter outbreaks, periodic, endemic, unpredictable pandemic infections. Symptoms include high fever, body aches, and fatigue. Coryza, cough, headache, prostration, malaise, and inflammation of the upper respiratory tree and trachea persist for 7 to 10 days, feeling Weakness and fatigue present for days to weeks).People of all ages are affected but school-age children and infants aged and physically unfits have disease severity. Croup /laryngotracheitis can be a serious complication in small children. From influenza A viruses, hemorrhagic bronchitis, pneumonia are sever complications in patients suffering from pulmonary or cardiac disease, or diabetes mellitus. Four pandemics of 20th century: Spanish influenza (H1N1) in 1918/1919(most devastating bacterial pneumonia), Asian influenza (H2N2) in 1957, Hong Kong influenza (H3N2) in 1968, and H1N1 influenza in 2009[28] worst influenza virus pandemic senario in 1918, killed approximately 50 million people worldwide[27,29]Influenza A H1N1is pandemic in 2009[27] and avian influenza (HPAI) virus of H5N1 causes highly pathogenic pandemic emergency[29] Reverse genetics of virus indicates its cloning[27]in 1999. IAV infects Alveolar macrophages that migrate to influenza-infected lungs play a pathogenic role in pulmonary inflammation. [27] Innate immunity have two distinct role while aduptive immunity (antigen specific antibody by T and B cells) recovers the host from infection and protect the host from reinfection.

➢ *DENGUE VIRUS:*

Dengue is an acute infectious , endemic[31,33](128 countries with indian subcontinents is epicenter) viral illness with self limiting fever(5-7days) to life threatening Dengue hemorrhagic fever(DHF) . Chinese medical encyclopedia from Jin Dynasty (265-420AD) which referred to a "water poison" by flying insects. Break Bone Fever was named by Benjamin Rush in 1789 (Philadelphia epidemic)named "bilious remitting fever". The term dengue fever came into use after 1828.[34] It is caused by RNA virus of family, has 4 serotypes: DENVs 1–4[33]. , spread by female Aedes Albopictus (DHF)[30,31,32] and Aedes Aegypty mosquitoes[33] bites. The life cycle of *Aedes* mosquito depending upon the extent of feeding lasts for 8–10 days at room temperature. It consists of two phases: aquatic (larvae, pupae) and terrestrial (eggs, adults) phase[31].In humans, the mosquito delivers virus in skin epithelium, infects and replicates in the cells of mononuclear lineage (monocytes, dendritic cells, macrophages, and Langerhans cells). These cells carry the virus to lymph nodes, where it replicates, viremia occurs. It is followed by systemic infection of liver, lungs, and spleen. Symptoms similar as typhoid or Typhoid Fever (TF) characterized by fever with body ache, nausea, vomiting, red skin spots [32], petechiae on extremities, respiratory symptoms , decreased apatite, nosebleeds! later DHF and dengue shock syndrome (DSS)in children, adolescents and adults [32]. Dengue fever still occur in

Indonatia every year[30]. Number of sufferers from 2014-2019 can involve heart, kidneys, brain, and lungs along with above mild symptoms to unstable breathing, fainting and death due to shock .DHF with critical plasma loss may be life threatening if not treated properly, characterized by a rapid, weak pulse with narrowing pulse pressure (<20mmofHg), cold clammy skin, and restlessness. The patient may die within 12–24 h of going into shock or recover rapidly with volume replacement therapy[31]. Life long immunity with any of serotypes after primary infection does not provide protection against other serotypes for secondary infection.[31] Till date no drug is available for dengue. Bed rest, oral rehydration, and paracetamol as an antipyretic and analgesic, Patient's health monitoring through blood tests from fever day 3 onwards,patient recovers within 12–48h of fluid therapy are performed till the condition improves Licensed Sanofi Pasteur dengue vaccine Dengvaxia is under trial of its success.31

- *ROTA VIRUS :*

It is Rotavirus genus of the Reoviridae of a Reoviridae Family , genome, composed of 11 segmented double stranded RNA. Its virion is complex, non enveloped and surrounded triple layered capsid.[35] It has six structural and six nonstructural protein. From A to E genus , A to C Infects humans and all infects animals. Age dependant immunity, so it is restricted upto children of 5 years/youngs.[36] Rotaviruses replicate in the nondividing mature enterocytes near the tips of the villi. Infection alters small intestinal epithelial motility function results in malabsorptive diarrhea and inflammation. Enterocyte vacuolization and loss or villus blunting due to ischemia and crypt hyperplasia , result in the transit of osmotically active undigested bolus of mono and disaccharides, carbohydrates, fats, and proteins into the colon. The colon is unable to absorb sufficient water, leading to an osmotic diarrhoea with viruses in stool10^{10} particles /gram. Malnutrition increases the severity of rotaviruses infection. Approved vaccines was recommended in an early 80's to 3rd Generation RotaTeq and Rotarix vaccines [37] but later withdrawn due to its adverse effects. Pathogenesis of Intestinal and Systemic rotavirus Infection depends on person's health, virus replications, reinfection , herd or individual immunity after primary infection.

- *SARS-COV:*

Severe acute respiratory syndrome (SARS) is an infectious viral disease of the lower respiratory tract. Corona viruses are enveloped, single-stranded of largest genome[40], positive-sense RNA viruses of coronaviridae [38]family. Virus replicates in upper respiratory tract. SARS coronavirus causes collapse of tracheobronchial alveolar epithelial cell by diffuse edema, desquamation[38], fibrosis, atrophy, thrombosis, necrosis[38], degeneration and apoptosis like deadly effects. Damage of several organs like brain, intestine, glands, spleen, lymphnodes, kidneys and immune cells injury was seems by all above deadly effects. No definite effects on bone marrow. The pathogenesis of SARS is highly complex seems that both abnormal immune responses and injury to immune cells with lack of ACE2 expression may have a key role . Multinucleated syncytial cells[38] are common histological structure found in many viral infection with no report of presence in H5N1 type infection[38].Viral antigen, nucleic acid and virions are found on the bronchiolar epithelial cells[38]. SARS was first emerged in China's Guangdong Province in November 2002[38], pandemic to epidemic between 2003 and sporadic till spring 2004. Bat species is the natural reservoir of virus. virus transmission to and among humans is by direct contact, droplet, and airborne and is isolated from cat ,dog like animal. Virus is isolated from faecal and urinary samples. Flu-like symptoms including fever, chills, cough, and malaise, with the 70% of the patients, suffer from shortness of breath and recurrent or persistent fever, whereas the 30% show improved after first week,20 to 30% of patients were required intensive care treatment with mechanical ventilation in 2003. Thrombocytopenia and lymphopenia [38] have been frequently detected in SARS patients and 6.8% fatality rate in younger than 43% in 60 years of age were the estimated autopsied reports since the first outbreak in 2003.

- *COVID -19 (2019-nCOV)*

COVID-19 is a new viral infection caused by the severe acute respiratory coronavirus 2 (SARS-CoV-2).SARS-CoV-2,a new coronavirus(*coronam*= crown)[41] found in WUHAN in december 2019[42] is of family *Coronaviridae*, subfamily *Coronavirinae, which have* solar corona[virion with 9-12 nm long spikes.[42] Virus is spherical 7th, non segmented , largest(18kb in length{27 to 32 kb}), spherical, enveloped, highly transmissible,[43]contagious, positive-stranded RNA virus[41,43] Amongst alpha, beta, gamma, and delta categaries, SARS-cov2 is of Beta family[41,42,43]. Encoding genome have multiple structural proteins for infection in host by fusion, assembly and formation of virus and non structural proteins for replication and transcription of virus . Envelop , membrane and spike proteins acquire its peculiar pathogenic properties[44] SARS(Severe acute respiratory syndrome)-CoV in 2003[43] , MERS (middle east respiratory syndrome)-CoV emerged in 2012,[43] and SARS-CoV-2 (WHO named COVID-19)deadly affect multiple organs along with severe respiratory illness. Pangolin and Bat are the reservoir of virus.

Out of six Human Coronavirus species (HCoV) , four of them are a causative virus for common cold symptoms in immunocompromised individuals. Anlytical genomes lineage A and C types were found in American and Europeans, while the B types was prevalent in East Asia might needs mutation for outer country spread. The lineage C was prevalent in France, Italy, Sweden, England, California, Brazil, Singapore, Hong Kong [43] Fever, cough ,fatigue and death are common symptoms of SARS coV2.[42] More complex and large clove shaped spikes proteins [43] [with internal fusion peptide, double cleavage sites, and long six-helix bundle [permit larger binding affinity of virus with host receptor ACE2(Angiotensin –converting enzyme 2)might explain faster spread of SARS-CoV-2 than that of SARS-CoV.[42] Above 20million confirmed cases with more than 7lakhs deaths(till date

written),brought major health emergency threats, social issues as well as drastic economical crisis, as of worldwide outbreak a pandemic.[43]

III. CONCLUSION

Any viral nucleic acid detected by PCR is actually infectious virus. Positive sense virus is similar to mRNA , immediately translated by host cells whereas negative – sense virus is complemantary to mRNA so before translation it must need to convert in positive sense .To degrade and recycle easily when genes are activated, RNA Has to transcribe and translate , RNA is single stranded for unstable nature. RNA virus have high mutation rates that allow fast evolution. RNA viruses have high rates of sequence divergence, small genomes recombination, and reverse transcription machinery. poilo virus was first man made virus generated without natural templet were of Polio virus and Q><174 bacteriophage.[40] Virus isolation by culture, histopathology, seroanalysis, molecular techniques of polymerase chain reaction (PCR),Reverse-transcriptionPCR and real-time PCR [39,40] are in use today. Stopping viral replication by target stopping of genetic process of cleaving /splitting the DNA/RNA strands will able to stop their correct functioning.

With a period of time, repeated infections in humans from bats, a reservoir of virus of coronaviridae family with structural changes showed different virulent effects. Infectious disease study review may guide and provide lessons to FOCUS more on to shift on anti disease approach adopted by bats rather than traditional anti pathogen approach to control infectious disease in humans.

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