A Comparison Study of Biology of Hepatitis C Virus (HCV), Human Immunodeficiency Virus (HIV) and Ebola Virus (EbV)

Chetan Datta Poduri

Department of Biotechnology (BT), SreeNidhi Institute of Science & Technology (SNIST), India

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Abstract In the past there were at least 23 epidemics with Ebola virus (EbV). Presently there are pandemics with Hepatitis C virus (HCV) and Human Immunodeficiency virus (HIV). The recent epidemic of EbV has taken an year to get contained. Infections with HCV and HIV are continuing to increase. At present, except for EbV, neither HCV nor HIV have a vaccine to prevent future infections. Here, a snapshot of the three viruses with regard to their characteristics and prevalence (both global and Indian) are generated with an emphasis to study the infection dynamics of these three RNA viruses in relation to each other. An emphasis is made towards the common or shared features of the three viruses.

Keywords HCV, HIV, Ebola, Characteristics, Prevalence

1. Introduction

Three RNA viral infections of humans – hepatitis c virus (HCV), human immunodeficiency virus (HIV) and Ebola virus (EbV) – are wrecking havoc on the mankind. Complicating this scenario is the absence of effective vaccines to prevent future infections with these viruses. Additionally, the best therapeutic strategy for managing patients with any of these three viral infections is to provide supportive care to the affected. Various characteristics of the three viruses are compared in Table 1.

Table 1. Comparison of characteristics of Hepatitis C virus (HCV), Human Immunodeficiency Virus (HIV) -1/-2 and Ebola viruses.

Virus →	Hepatitis C virus (HCV)	Human Immunodeficiency virus (HIV) - 1	Human Immunodeficiency Virus (HIV) - 2	Ebola Virus (EbV)
Discovery	1989	1983	1986	1976
First Indian Report	1992	1986	1991	2014
Family	<i>Flaviviridae</i>	<i>Retroviridae</i>	<i>Retroviridae</i>	<i>Filoviridae</i>
Genus	Hepacivirus	Lentivirus	Lentivirus	Ebola-like Viruses
Natural Hosts	Vertebrates	Vertebrates	Vertebrates	Vertebrates
Characteristic/Property				
Particle	Presumed Icosahedron	Spherical - pleomorphic	Spherical - pleomorphic	Pleomorphic
Size	40 - 60 nm	80 - 100 nm	80 - 100 nm	80 x 970 nm
Genome	RNA/linear	RNA/dimer	RNA/dimer	RNA/linear
Sense	+	+	+	(-)ve
Segmented	No	No	No	No
Length	~9.4 kb	~10 kb	~10 kb	~11 kb
Copies	One	Two	Two	One
ORF	One/Alternate frame reported	9	10	One
Replication Strategy	Group IV	Group VI	Group VI	Group V
Genotypes	~ 8 identified	~ 8 identified	~ 8 identified	~ 5 reported
Recombinant forms	Reported	Reported	Reported	To be reported
Proteins	10	15	17	7 (yet to be completely characterized)
Structural Proteins	3	2	2	--
Non-structural	7	13	15	--
Receptor	LDL/CD 81(?)	CD 4	CD 4	DC-SIGN/DC-SIGNR(?)
Co-receptor/assistant molecules	Cholesterol transporter Niemann-Pick C1 (NPC1) (?)	CXCR 4 &CCR 5	CXCR 4 &CCR 5	Cholesterol transporter Niemann-Pick C1 (NPC1) (?)
Transmission	Nosocomial, contaminated body fluids and organs	Contaminated body fluids, Majority by sexual transmission	Contaminated body fluids, Majority by sexual transmission	Vector-borne, Sexual. Humans dead-end hosts
Vector	--	--	--	Mosquitoes
Natural Reservoir	Primates (?)	Primates (?)	Primates (?)	Fruit bats
Clinical Disease	Hepatitis and associated liver disorders	AIDS	AIDS	Majority asymptomatic, Neurologic symptoms
Treatment	Typically Interferon	ART	ART	Ebola Supportive care
Vaccine	--	--	--	Phase II trials
Additional Information	--	--	--	Category A bioterrorism agent

Legend.**Abbreviations used:**

AIDS - Acquired immunodeficiency syndrome; ART - Antiretroviral therapy; kb - kilobases; LDL - low density lipoprotein; nm - nanometer; RNA - Ribonucleic acid; Other abbreviations carry their usual significance.

Sources:

Brown, R. S., and Gaglio, P. J., *Liver Transpl*, 2003; **9**: s10 - s13; Cann, A. J., *Principles of Molecular Virology*, 3rd Ed. Elsevier Academic Press, UK, 2004; Carette, J. E., et al. *Nature*, 2011; 477(7364): 340; Cristiani, N., HIV Example of quantitative analysis of natural selection. 2006. www.computational-genomics.net/case_studies/hiv_demo.html; *J Gen Virol*, 2014; **95**: 1619 - 1624; Kesters, L., *Virology and Immunology of HIV*. www.itg.be 2015; Lindenbach, B. D., and Rice, C. M., *Nature Rev Microbiol*, 2013; **11**: 688 - 705; Muyembe-Tamfum, J. J., et al. *Onderstepoort J Vet Res.*, 2012; **79** (2), Art# 45, 8 pages. <http://dx.doi.org/10.4102/ojvr.v79i2.45>; *Nature*, 2014, **514**, 554 - 557; Passi, D., et al., *J Clin Diagn Res*, 2015; **9** (6): LE01 - LE06; *The Gale Encyclopaedia of Science Vol 2*. Web; viralzone.expasy.org; www.cdc.gov - About Ebola Virus disease; www.hivlanl.gov; www.springer.com - Spotlight on Ebola; www.viprbtc.org; www.who.int/Ebola; Yu, X. F., *Nature*, 1988; 335(6187): 262 - 265.

Despite differences in replication strategies and the pathogenesis patterns of the three viruses, we can easily identify from table 1 that the viruses when compared in pairs have something in common apart from the genome being RNA. This can be depicted as a Venn diagram as in Figure 1.

Legend. The overlapping regions identify common/shared properties of the respective viruses. All abbreviations carry their usual significance.

Figure 1. Venn diagram depicting the common aspects of three viruses in the present study – HCV, HIV & EbV.

2. Materials and Methods

Because the three mentioned viruses have RNA as their nucleic acid, and seem to be infecting a large number of human populations, it makes sense to study these three viruses together. With this as the aim, scientific literature was scanned through for prevalence of infection with any of the three viruses since 1976. For this purpose multiple search engines and internet resources were used to access full articles. These include google scholar, PubMed, and Gale's Academic OneFile InfoTrac (provided through author's personal membership of British Council Library, Hyderabad, India). Only those articles for which the author had full-text access were included. Data made available in abstracts for which the author could not have complete article access were not included in the present study. Statistics with regard to the world are collated as Table 2, while Table 3 summarizes similar statistics with regard to India.

Table 2. Global decadal statistics for Hepatitis C virus (HCV), Human Immunodeficiency Virus (HIV) – 1 & 2, and Ebola virus (EbV).

Decade	Prevalence (unless indicated all values are average of values reported in various sources)			
	Ebola virus (EbV)	Hepatitis C virus (HCV)	Human Immunodeficiency virus (HIV) – 1	Human Immunodeficiency virus (HIV) – 2
1976 – 1985	637	Not discovered	20,303	Not discovered
1986 – 1995	370	122 million	> 3 million	
1996 – 2005	832	176.85 million	32.2 million (on 2005)	
2006 – 2015	25,987	158 million	37.7million (at March, 2015)	
Sources: Alter, M. J., <i>World J Gastroenterol</i> , 2007; 13 (17): 2436 – 2441; Hanafiah, K. M., <i>et al.</i> , <i>Hepatology</i> , 2013; 57 : 1333 – 1342; Lavanchy, D., <i>Clin Microbiol Infect</i> , 2011; 17 : 107 – 115; www.avert.org ; www.unaids.org ; www.who.int ; Yee, T. T., <i>et al.</i> , <i>Gut</i> , 2000; 47 : 845 – 851.				

Table 3. Indian decadal statistics for Hepatitis C virus (HCV), Human Immunodeficiency Virus (HIV) – 1 & 2, and Ebola virus (EbV)

Decade	Prevalence (unless indicated all values are average of values reported in various sources)			
	Ebola virus (EbV)	Hepatitis C virus (HCV)	Human Immunodeficiency virus (HIV) – 1	Human Immunodeficiency virus (HIV) – 2
1976 – 1985	○	Not discovered	○	Not discovered
1986 – 1995	○	6.69 million (estimated)	2108 (people with AIDS)	
1996 – 2005	○	9,783,000 (on 2004)	5.1 million (on 2003)	
2006 – 2015	1	18,216,960 (on 2010)	2.5 million (2005) → 4.4 million (at 2013)	

Note: NACO started AIDS/HIV surveillance in 1998, prior to which screening at various limited designated places in India was done by ICMR since 1986.

Sources:
 Acharya, S. K., *et al.*, *Natl Med J India*, 2006; **19** # 4: 203; Bagochi, S., *BMJ* 2014; **4**; 349: g7328; Factsheets on HIV/AIDS and sexually transmitted infections. India. Update 2004. www.who.int; Hepatitis C: surveillance and control. Global Alert and Response (GAR). World Health Organization. 2015. Web. www.who.int; HIV Data. Updated 18-Nov-2015. Accessed 18-Nov-2015. Naco.gov.in; Lavanchy, D., *Clin Microbiol Infect*, 2011; **17**: 107 – 115; Ramesh, R., *et al.*, *J Gastroenterol Hepatol*, 1992; **7**: 393; Shepard, C. W., *et al.*, *Lancet Infect Dis*, 2005; **5**: 558 – 567; www.avert.org.

3. Observations, Results & Discussion

Readers must note at this stage that whereas EbV was discovered in 1976, only in the latter half of 1980s were the other two viruses (HCV & HIV) discovered. While HIV-1 was discovered in 1983, HIV-2 was discovered in 1986. 1989 saw the discovery of HCV. Therefore prior to 1976 there were no reports of any of these three viruses. However, some information with regard to HCV might be available as documented under the old name Post transfusion non-A, non-B hepatitis (PT-NANBH). Again with the discovery of two more viruses the GBV-C in 1995 [1], and transfusion transmitted virus (TTV) in 1997 [2], cases of PT-NANBH cannot be exclusively classified as HCV. Therefore, certain amount of doubt exists with regard to the same and hence 1976 was taken as the starting point for generating information in tables 2 and 3.

From Table 1 it is readily observable that both HCV and EbV share cholesterol transporter as one assistor molecule for the entry of their respective viral particles into cells [3, 4]. It must be noted at this stage that various authors have noted that HCV appears to be an opportunistic pathogen in HIV infection. Needless-to-say, at present 4 – 5 million people living with HIV/AIDS are also co-infected with HCV [5, 6]. Also, all the three viruses seem to share at least one common mode of transmission that of transmission from humans to humans via contaminated body fluids and contaminated organs used for transplantation. In other words, these viruses seem to share at least nosocomial mode of transmission. When considered in pairs, HIV and EbV share an additional sexual mode of transmission.

Furthermore, at least two reports suggest that bats might be one possible natural reservoir for HCV [7, 8]. Incidentally, bats are the natural reservoirs for EbV (Table 1). Despite the genera of bats, the very observation that this animal is the reservoir for HCV and EbV has potential implications given the fact that recombination among RNA viruses is documented to be a relatively common event. And inter-genera crossings among bats might be occurring naturally whence a few bats may harbor both the viruses simultaneously. Therefore, there is a clear need to study infection dynamics of HCV, HIV and EbV together. Such a study would involve simultaneous monitoring of anti-viral antibodies against HCV, HIV and EbV in the patient sera. With the increased acceptance of antibody diagnosis of viral infections, whereas cross-reacting antibodies may give a false picture, a true snapshot is obtained only when the corresponding antigen is isolated from the patient samples. However, it may be noted that for viruses like HCV and HIV, perhaps the only acceptable antigen isolation for routine testing is in nucleic acid tests (NAT) in the form of reverse transcription polymerase chain reaction (RT-PCR) which can be made quantitative in many cases. Also, identifying the infecting genotype, at least for research purposes, for monitoring the evolutionary dynamics of the virus becomes an essential element when HCV is involved.

In addition to what has been described above, although EbV seems to survive in the wild in (fruit) bats, a number of other animals have been shown to harbor the virus. These include guinea pigs, goats, horses, dogs [9] and pigs (*Sus scrofa*) [10]. However, among these, as Allela *et al* suggest, perhaps only dogs seem to be naturally and

asymptomatically infected with EbV [9]. Put simply, the entire natural host range of EbV is yet to be mapped; and primary transmission seem to be occurring in animals, with animal-to-human or human-to-human transmission representing a secondary transmission for EbV. Given these observations, it could be possible that the virus might be still evolving and may likely to acquire novel characteristics. Partial evidence for this statement comes from the observation that the infecting strains of EbV in DRC and West Africa appear to be different in the recent epidemic of Ebola in Africa [11]. Similar arguments can be extrapolated to HCV and HIV with specific reference to the natural host range.

Till date only co-infection cases of either HCV – HIV, HIV – EbV and/or EbV – HCV have been reported. Although specific co-infection cases of EbV and HCV are yet to be identified, efforts by earlier researchers in this direction does indicate the possibility towards such infections [12]. The possibility of HIV-EbV co-infection arises as a consequence of isolation of HIV from archival samples of EbV in retrospective studies [13]. However, Parkes-Ratanshi *et al* do report the presence of viral hemorrhagic fever (VHF), albeit of a varied etiology, in patients visiting an HIV centre [14]. They also mention that such a situation represents on high risk threat in areas with high HIV population. To the best of the author's knowledge reports of super infections with all the three viruses in a single individual are yet to be documented. Despite this, as mentioned earlier, viruses recombining amongst themselves or with other viruses either in the wild within the identified natural carriers or in nosocomial settings when the contaminated body fluids are administered to patients cannot be ruled out entirely. Therefore, even in the absence of any patient specific data or animal studies, compulsory monitoring of all individuals reporting for various ailments to healthcare personnel at least in the Ebola affected countries of Democratic Republic of Congo (DRC), Liberia, Nigeria, Sierra Leone and other potentially threatened African countries becomes essential. Thus, continuous monitoring of sylvatic animals, in addition to determining the complete host range of the three viruses, although a difficult proposition, in the mentioned directions is the need of the hour.

Endnote/Acknowledgements

Data presented in Tables, and a poster presented by the author at the 14th FAOBMB congress & 84th SBC (I) meet held at Hyderabad, India between 27th – 30th November, 2015, share the same data.

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Author's mailing address/contact details: Flat – 501, Highlight Haveli, Street – 6, Habsiguda, Hyderabad – 500007, Telangana, India. Phone(s): +91-9492891303 & +91-9816160830.

List of Abbreviations

AIDS – Acquired immunodeficiency virus; DRC – Democratic Republic of Congo; EbV – Ebola virus; HCV – hepatitis C virus; HIV – Human immunodeficiency virus; NAT – nucleic acid testing; PT-NANBH – Post-transfusion non-A, non-B hepatitis; RNA – Ribonucleic acid; RT-PCR – reverse transcription polymerase chain reaction; TTV – Transfusion transmitted virus; VHF – Viral hemorrhagic fever; Other abbreviations carry their usual significance.

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