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Host characteristics and their influence on zoonosis, disease emergence and multi-host pathogenicity

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ABSTRACT

The interplay between agent-host-environment characteristics is responsible for the emergence and zoonotic potential of infectious disease pathogens. Many studies have investigated key agent characteristics and environmental factors responsible for these phenomena. However, little is known about the role played by host characteristics in zoonoses, disease emergence and the ability of pathogens to infect multiple hosts. We compiled a dataset of 8114 vertebrate host–agent interactions from published literature. Multiple host characteristics and the pathogen's zoonotic, emergence and multi-host potential were then linked to the dataset. The associations between zoonotic, emerging human pathogen and multi-host pathogenicity and several host characteristics were explored using logistic regression models. The numbers of publications and sequences from the agent–host combinations were used to control for the research effort. Hosts in the class Aves (odds ratio [OR] 20.87, 95% CI 2.66–163.97) and Mammalia (OR 26.09, 95% CI 3.34–203.87) were more likely to host a zoonotic pathogen compared to the class Amphibia. Similarly, hosts having Bursa fabricii (i.e., birds) (OR 1.8, 95% CI 1.4–2.3) were more likely to host an emerging human pathogen. The odds of being a zoonotic pathogen were highest when the host female required a greater number of days for maturity, and the pathogen was able to affect a greater number of host species. In contrast, the hosts from which a higher number of pathogens were reported were less likely (OR 0.39, 95% CI 0.31–0.49) to be associated with an emerging human pathogen. The odds of an emerging human pathogen were highest when the host had a higher adult body mass, and the specific pathogen could affect more host species. The odds of a pathogen infecting multiple hosts were highest when a host had shorter female maturity days (>670–2830 days) and lower birth/hatching weight (>42.2–995 g) compared to longer female maturity days (>2830–6940 days) and greater birth/hatching weight (>3.31–1160 kg). We conclude that several host characteristics – such as mass, maturity, immune system and pathogen permissiveness- are linked with zoonoses, disease emergence or multi-host pathogenicity. These findings can contribute to preparedness for emerging infections and zoonotic diseases.

1. Introduction

Over the past few decades, there has been a persistent rise in the emergence of infectious diseases [1]. These emerging infectious diseases (EIDs) pose a significant and imminent threat to the health of both humans and animals on a local and global scale [2]. In particular, numerous pathogens responsible for infectious diseases in wildlife continue to pose an ongoing risk of transmission to human and domestic animal populations [3]. A striking example of this phenomenon is the recent emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from wildlife, leading to the worldwide COVID-19 pandemic [4]. Addressing the challenge of emerging zoonotic diseases has become a paramount concern for global public health [5], prompting the adoption of the One Health approach as a means to effectively combat these diseases [6].

Most of the pathogens infecting animals and humans are multi-host pathogens [7]. Multi-host pathogens have been reported to be more likely to have the capabilities essential for disease emergence [8]. The impact of multi-host pathogens is difficult to mitigate due to their complex transmission pathways or dispersal mechanisms [9]. High genetic diversity and ample opportunities for cross-species transmission are important factors responsible for the multi-host pathogenicity of

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infectious agents [7]. However, there has not been much research on the importance of specific host characteristics on the ability of pathogens to infect multiple hosts.

Socio-economic, ecological and environmental factors are believed to influence the disease emergence [10]. Enhanced EID risk has been reported in forested regions experiencing land-use changes and high wildlife diversity [5]. Recently, we demonstrated that inherent virus characteristics, host range, geodemography, and societal and environmental factors are linked with zoonosis and disease emergence [11,12]. Based on the multifactorial host-agent-environment interface theory of disease emergence and zoonosis, a suitable agent-host combination is essential in this process. However, compared to pathogen virulence, host factors are often ignored. Understanding host responses and the phenomena of species barriers that lead to benign or lethal infections in different hosts is urgently required [13,14]. Detailed analyses to understand the association between key host characteristics and disease emergence, zoonosis and multi-host pathogenicity are lacking. Here, we analyse the potential role of key host characteristics in disease emergence, zoonoses and multi-host infections.

2. Methods

In brief, we compiled a dataset of vertebrate host–zoonotic/human emerging/multi-host pathogen and host characteristics. First, we compiled a vertebrate host–agent dataset from published literature. Multiple host characteristics were then linked with each host species. After this, the pathogens were categorised as zoonotic/nonzoonotic and emerging/nonemerging. Information related to the number of hosts from which a pathogen has been reported, and the number of pathogens reported from a host was also compiled. Lastly, the association between zoonotic/emerging/multi-host levels of pathogens and several host characteristics was explored. Detailed methods are described below.

2.1. Vertebrate host–agent dataset

To compile this data, we used the species-species interactions dataset developed by Wardeh and colleagues [15]. This database has 22,515 unique species interactions among 6314 hosts (carrier) species and 8905 agents (cargo) species.

The interactions involving a virus (4190), viroid (93), bacteria (7963), fungi (2195), helminth (3375), protozoan (1458) and other (71) agents were retained. The interactions involving agents such as arthropods (2762), brown algae (2), bryozoan (2), cnidaria (326), diatom (2), golden algae (1), green algae (8), higher plants (1), Mollusca (4), segmented worm (19) and water mould (43) were discarded. This resulted in the selection of 19,345 agent-host interactions.

From the 19,345 agent-host interactions, the interactions involving amphibians (191), Aves (1326), domestic animals (3134), fish (2547), humans (1631), mammals (1551), primates (427), reptiles (235), rodents (578) and other hosts (44) from the above-described 19,345 unique agent-host interactions were retained. This resulted in selecting 10,406 agent-host interactions from 19,345 unique agent-host interactions.

There were 4468 agents and 2264 hosts resulting in 10,406 agent-host interactions. From this dataset, a unique list of 2264 host names was obtained. Host organisms in class “Others” were individually scrutinized and classified as either vertebrate or invertebrate hosts. The interactions involving invertebrate hosts were discarded. This resulted in the selection of 2238 host and 4431 agent species and 10,363 agent-host interactions.

Host-specific data were represented within 14 different host classes. However, due to the non-availability of host characteristic data, the hosts belonging to fish classes (Actinopterygii, Cephalaspidomorphi, Chondrichthyes, Chondrostei, Cladistei, Dipnoi, Elasmobranchii, Holocephali, Holostei, and Teleostei) were not used in the analyses. In addition, 144 hosts that lacked host class information were also discarded. These procedures resulted in a final set of 8114 agent-host interactions.

2.2. Host-specific parameters

The taxonomic classification of hosts was recorded. Host classes mentioned in Wardeh, Risley (15) were retained. In addition, two new variables - ‘Human/Nonhuman’ and ‘Domestic/Nondomestic animal hosts’ - were created from this host classification data. The domestic vertebrate animal hosts consisted of 45 species of domestic food animals, companion (pet) animals, and exotic (food or pet) animals [15,16].

The taxonomic classification (Class, Order, Family) data for 1165 hosts were extracted from AnAge, The Human Ageing Genomic Resources (HAGR) [17], also available at: http://genomics.senescence.info/download.html#anage. Host class, family and order data were also recorded from LPI [18]. For the remaining hosts, host class, order and family data were recorded from the Integrated Taxonomic Information System online database, http://www.itis.gov (Retrieved [01, 19, 2019]).

Immune system related information for different host classes was also recorded [19–23]. The immune system associated characteristics included amniote, body temperature control (endotherm/ecotherm), and bursa fabricii. Birds have bursa fabricii, which is absent in the amphibians, reptiles and mammals. Birds and mammals are endotherms (have the ability to regulate their body temperature), whereas amphibians and reptiles are ectothermic (dependent on the external environment to regulate their body temperature) in nature. Reptiles, birds and mammals are amniote as compared to amphibians. The embryo in the amniotes develops inside the protective extra-embryonic membranes (amnion, chorion, and allantois).

Important parameters available for hosts - such as maximum longevity (years), female maturity (days), gestation/incubation (days), litter/clutch size, birth or hatching weight (g), and adult body mass/weight (g) - were extracted from Myhrvold, Baldridge (24). In addition, the missing data for gestation/incubation (days), litter/clutch size, birth weight (g), adult weight (g), and maximum longevity (years) were further updated [17], also available at AnAge, The Human Ageing Genomic Resources (HAGR); http://genomics.senescence.info/download.html#anage. In cases in which there were some variations in the parameters in the AnAge dataset [17] and that of Myhrvold, Baldridge [24], the parameters in the Myhrvold, Baldridge [24] dataset were retained.

The variables adult weight (gm) and adult body mass (gm) were considered similar and additional information available in [17] was added. Two more variables were also created from the existing data: a) multi-pathogen level of a host (the number of pathogens identified via sequencing (either partial or complete) from a host; for example, 418 pathogens sequenced from *Bos taurus*); and b) multi-host level of a pathogen (the number of hosts from which a pathogen has been identified using sequencing; for example, *Bacillus anthracis* sequenced [partial or complete sequences] from 9 hosts).

Host-specific characteristics of certain species were also used for their sub-species. For example, *Canis lupus* for *Canis lupus familiaris*; *Equus asinus* for *Equus asinus africanus; Mus musculus* for *Mus musculus domesticus; Mustela putorius* for *Mustela putorius furo;* and *Sus scrofa* for *Sus scrofa domesticus/ Sus scrofa leucomystax/ Sus scrofa scrofa.*

2.3. Zoonotic and emerging pathogens

Zoonotic pathogens included those reported from humans and [other] vertebrates [15], except that pathogens reported only from humans in the database, such as kyasanur forest disease virus, *Taenia asiatica* and *Trichinella nelsoni* - were also included. The natural transmission potential between humans and [other] vertebrates of all these pathogens could not be verified. The emerging pathogen status of all the

infectious agents was classified as previously reported [8,25]. In addition, human viruses that emerged during the past 20 years — such as severe acute respiratory syndrome virus and MERS corona virus — were included [26,27]. Overall, the final dataset contained 637 zoonotic and 145 emerging human pathogens.

2.4. Data analyses

All statistical analyses were conducted in R [28].

2.4.1. Predictors and outcomes

Host characteristics were used as key predictors. Overall, 11 predictor variables were explored in the analyses. In addition, the variables 'multi-pathogen level of a host' and 'multi-host level of a pathogen' were considered predictor variables for zoonotic and emerging human pathogen status outcome modelling, and the zoonotic status of a pathogen was used as a predictor variable for emerging human pathogen outcome modelling. The number of publications and sequences from the agent–host combinations were used to control for the research effort.

The detection of a zoonotic, emerging human pathogen from a vertebrate host species, and the multi-host level of a pathogen were considered to be outcome variables.

2.4.2. Descriptive analyses

Single variable analyses of all the variables were conducted, followed by bivariate descriptive analyses of all predictors with the three outcome variables. Continuous variables were categorised by binning them at their quartiles when the conditions of linearity were not met.

2.4.3. Univariable logistic regression analyses

Univariable logistic regression analyses of predictor variables with outcome variables were conducted. Considering that 8114 host-agent interactions were explored, variables with a chi-square p-value of <0.25 and $<15\%$ missing values were retained for further multivariable modelling. We used generalised variable inflation factors (GVIF) to identify multicollinearity and eliminated variables with a GVIF^(1/(2*Df)) >2 and GVIF >5 from further modelling.

2.4.4. Multivariable logistic regression analyses

Multivariable analyses were conducted using generalised linear models for three outcome variables. A forward stepwise approach was used, and the models were fit by maximum likelihood with binomial errors. Initially, the variables with $P < 0.05$ were retained and all the non-significant variables were re-tested in the final model. Odds ratios were used to quantify associations between predictor and outcome variables. Biologically important two-way interactions among the predictor variables in the final model were tested and significant interactions were retained. Model adequacy was tested using the chi-squared goodness-of-fit statistic, McFadden's R squared, and the Durbin Watson test.

3. Results

3.1. Descriptive analyses

Overall, 8114 host-agent interactions were categorised. There were 3933 zoonotic and 1485 emerging human pathogen status interactions. In the host-agent interaction dataset, the pathogen was reported from 1 to 4 ($n = 4168$) and $>$ 4–163 ($n = 3946$) hosts. The hosts in the host-agent interactions belonged to the classes Amphibia (184), Aves (1094), Mammalia (6626), and Reptilia (210). Detailed information regarding host characteristics and the number of sequences/publications per host-agent interactions are presented in the Supplementary Appendix, Table S1. Note that all the continuous variables were converted to categorical variables because the continuous variables were nonlinear variables.

3.2. Association of host characteristics with the zoonotic pathogen status outcome

Univariable results of the association of host characteristics with the zoonotic pathogen status outcome are reported in the Supplementary Appendix, Table S2. All variables except the comparison between birds and other host classes (amphibians, reptiles and mammals) were significant in the univariable analysis. After controlling for research effort, hosts in the class Aves and Mammalia, and those reporting a higher number of pathogens were significantly associated with a zoonotic pathogen outcome. The research effort variables - the number of publications and sequences published from a host-pathogen combination - also had a significant impact on the final multivariable model (Table 1). Statistical interactions indicated that the odds of having a zoonotic status were higher when the host female required a greater number of days for maturity, and the given pathogen was able to affect a greater number of host species (Table 2).

3.3. Association of host characteristics with the emerging human pathogen status outcome

All the predictor variables (host characteristics) had significant associations with the emerging human pathogen status in univariable analyses (Supplementary Appendix, Table S3). After controlling for

Table 1
Final multivariable model for a zoonotic outcome in a study of 8114 host-agent combinations. The effects of variables involved in significant interactions and interaction terms are presented in Table 2.

Category	Variable	Parameter estimate (b)	SE (b)	Odds ratio (95% CI)	p-value
Class	Amphibia	Referent			< 0.001
	Aves	3.04	1.05	20.87 (2.66, 163.97)	
	Mammalia	3.26	1.05	26.09 (3.34, 203.87)	
	Reptilia	1.98	1.09	7.25 (0.86, 60.88)	
Female maturity (days)	23.8, 334	Variable involved in a significant interaction			
	>334, 670 >670, 2830 >2830, 6940				
Multi-pathogen level of host	1, 117	Referent			< 0.001
	118, 1610	0.49	0.09	1.63 (1.36,1.95)	
Multi-host level of pathogen	1, 4	Variable involved in a significant interaction			
	>4, 163				
Number of sequences published	0, 1	Referent			0.041
	>1, 2	−0.19	0.09	0.83 (0.69, 1)	
	>2, 6	−0.01	0.08	0.99 (0.84, 1.17)	
	>6, 164,685	−0.17	0.07	0.84 (0.73, 0.97)	
Number of publications	0	Referent			< 0.001
	>0,8	0.52	0.08	1.68 (1.43, 1.98)	
	>8, 14,322	0.78	0.09	2.19 (1.85, 2.59)	

AIC value = 7117.43; McFadden's R squared = 0.37 (df = 17); SE = Standard error.

Table 2
Interactions significant in a final multivariable model for a zoonotic outcome in a study of 8114 host-agent combinations. The main effects of the variables not involved in interactions are presented in Table 1*

First variable	Second variable	Odds ratio (95% CI)	p-value
Female maturity (days)	Multi-host level of a pathogen		
23.8, 334	1,4	0.025 (0.01–0.04)	<0.0001
>334, 670	1,4	0.02 (0.01–0.04)	<0.0001
>670, 2830	1,4	0.01 (0.008–0.02)	<0.0001
>2830, 6940	1,4	0.02 (0.01–0.04)	<0.0001
[23.8, 334	>4163	0.42 (0.26–0.68)	0.0004
>334, 670	>4163	0.30 (0.19–0.49)	<0.0001
>670, 2830	>4163	0.32 (0.20–0.52)	<0.0001
>2830, 6940	>4163	1·0 (Reference)	

* ORs adjusted for other variables present in the model.

research effort, hosts having a Bursa fabricius, i.e., birds, those from which a lower number of pathogens were reported or pathogens reported to have a zoonotic outcome status were significantly associated with an emerging human pathogen outcome (Table 3). As above, the research effort variables were also significant in the final multivariable model (Table 3). Statistical interactions indicated that the odds of having an emerging human pathogen status increased when the host had a higher adult body mass, and the given pathogen was able to affect a greater number of host species (Table 4).

3.4. Association of host characteristics with a multi-host level of a pathogen status outcome

All the predictor variables had significant associations with the multi-host level of a pathogen in the univariable analysis (Supplementary Appendix, Table S4). After controlling for research effort, hosts having a Bursa fabricius, i.e. birds were more likely to host multi-host pathogens (Table 5). Statistical interactions indicated that the odds of having a pathogen infecting multiple hosts were higher when a host had lower female maturity days and lower birth/hatching weight (Table 6).

4. Discussion

We compiled a database of 8114 host-agent interactions. Important host characteristics were linked to investigate their role in their zoonotic, emerging and multi-host infecting capabilities. As far as we are aware, only a few studies have been conducted to understand the role of host characteristics in zoonosis, disease emergence and multi-host pathogenicity.

The hosts in the class Aves and Mammalia were more likely to host a zoonotic pathogen compared to the class Amphibia. Phylogenetic relatedness to humans and host taxonomy have been reported to be associated with the zoonotic potential of many virus species [29], and animal host genetics have been reported to play an important role in determining the zoonotic potential of pathogens [30]. Previous studies also indicate that mammals, followed by birds, are the crucial hosts for zoonoses [31].

Birds (hosts having Bursa fabricii) (OR 1.8, 95% CI 1.4–2.3) were more likely to host an emerging human pathogen. Free-living and migratory birds can carry pathogens over longer distances [32], therefore, there is always a risk of transmission of pathogens in novel foci or in naïve human populations. Live-bird markets have also been reported to be an important source of disease emergence [33]. Climate change and human movements have also been reported to play a significant role in avian-mediated human disease emergence [34]. Many emerging pathogens - such as influenza A virus, West Nile virus [32] and severe acute respiratory syndrome virus [35] - have been reported to be associated with wild birds.

Table 3
Final multivariable model for an emerging human pathogen outcome in a study of 8114 host-agent combinations. Effects of variables involved in significant interactions and interaction terms have been presented in Table 4.

Category	Variable	Parameter estimate (b)	SE (b)	Odds ratio (95% CI)	p-value
Zoonotic outcome	No	Referent			< 0.001
	Yes	3.18	0.15	24.13 (17.93, 32.48)	
Bursa fabricii	No	Referent			< 0.001
	Yes	0.59	0.13	1.8 (1.4, 2.3)	
Adult body mass (g)	2.4, 1120	Variable involved in significant interaction			
	>1120, 45,000				
	>45,000, 65,300				
	>65,300, 23,000,000				
Multi-pathogen level of host	1, 117	Referent			< 0.001
	118,1610	−0.94	0.12	0.39 (0.31, 0.49)	
Multi-host level of pathogen	1,4	Variable involved in a significant interaction			
	>4163				
Number of sequences published	0,1	Referent			< 0.001
	>1,2	−0.18	0.13	0.83 (0.65, 1.07)	
	>2,6	−0.02	0.10	0.98 (0.8, 1.2)	
	>6, 164,685	0.58	0.09	1.79 (1.51, 2.12)	
Number of publications	0	Referent			< 0.001
	>0,8	−0.05	0.12	0.95 (0.75, 1.2)	
	>8, 14,322	0.74	0.11	2.1 (1.69, 2.6)	

AIC value = 4865.54; McFadden's R squared = 0.37 (df = 16); SE = Standard error.

Similarly, after controlling for research effort, birds were more likely to host multi-host pathogens. Wild birds are known to travel long distances, and their ability to adjust to most habitats with the potential to act as bridge hosts might be associated with their capability to multi-host pathogens. As multi-host pathogens have been linked with disease emergence, avian species should be used as sentinels for disease emergence.

The hosts reporting a higher number of pathogens were significantly associated with a zoonotic pathogen outcome compared to those reporting a lower number of pathogens. Being a specific host population pathogen is likely to limit the pathogen's ability to infect other host populations [7,36,37]; serial passage experiments have supported this phenomena [38]. Multi-host pathogens have been reported to have higher opportunities for cross-species transmission [37], and these pathogens have the ability to use multiple modes of transmission with the potential for switching or shifting their host range [39]. Statistical interactions indicated that the odds of having a zoonotic status were

Table 4
Interactions significant in a final multivariable model for an emerging human pathogen outcome in a study of 8114 host-agent combinations. The main effects of the variables not involved in interactions are presented in Table 3*.

First variable	Second variable	Odds ratio (95% CI)	p-value
Adult body mass (g)	Multi-host level of a pathogen		
2.4, 1120	1, 4	0.130 (0.0736–0.230)	<0.0001
>1120, 45,000	1, 4	0.123 (0.0743–0.204)	<0.0001
>45,000, 65,300	1, 4	0.327 (0.2382–0.448)	<0.0001
>65,300, 23,000,000	1, 4	0.182 (0.1120–0.295)	<0.0001
2.4, 1120	>4, 163	1.166 (0.9209–1.477)	0.202
>1120, 45,000	>4, 163	0.874 (0.7088–1.079)	0.2109
>45,000, 65,300	>4, 163	0.641 (0.4915–0.836)	0.0011
>65,300, 23,000,000	>4, 163	1·0 (Reference)	

* ORs adjusted for other variables present in the model.

Table 5
Final multivariable model for a multi-host level of a pathogen outcome in a study of 8114 host-agent combinations. Effects of variables involved in significant interactions and interaction terms have been presented in Table 6.

Category	Variable	Parameter estimate (b)	SE (b)	Odds ratio (95% CI)	p-value
Bursa fabricius	No	Referent			< 0.001
	Yes	0.45	0.13	1.57 (1.22,2.02)	
Female maturity (days)	23.8, 334	Variable involved in a significant interaction			
	>334, 670				
	>670, 2830				
	(2830, 6940				
	0.013, 42.2	Variable involved in a significant interaction			
	>42.2, 995				
	>995, 3310				
Birth/ Hatching weight (g)	>3310, 1,160,000				
	0, 1	Referent			< 0.001
	>1, 2	−0.04	0.09	0.96 (0.81,1.14)	
Number of sequences published	>2, 6	0.13	0.08	1.14 (0.98,1.32)	
	>6, 164,685	0.60	0.07	1.82 (1.59,2.08)	
	0	Referent			< 0.001
	>0, 8	0.16	0.07	1.17 (1.01,1.36)	
Number of publications	>8, 14,322	1.11	0.07	3.05 (2.64,3.51)	

AIC value = 8254.85; McFadden's R squared = 0.27 (df = 22); SE = Standard error.

highest when the host female required a greater number of days (2831–6940) for maturity, and the pathogen was able to affect a greater number (5–163) of host species. This is expected; for example, *Homo sapiens*, as a host species, possess both of these characteristics.

Table 6
Interactions significant in a final multivariable model for a multi-host level of a pathogen outcome in a study of 8114 host-agent combinations. The main effects of the variables not involved in interactions are presented in Table 5*.

First variable	Second variable	Odds ratio (95% CI)	p-value
Female maturity (days)	Birth/Hatching weight (g)		
23.8, 334	0.013, 42.2	2.70 (1.3192–6.00)	0.007
>334, 670	0.013, 42.2	2.64 (1.2658–2.588)	0.010
>670, 2830	0.013, 42.2	3.20 (1.4328–7.00)	0.005
>2830, 6940	0.013, 42.2	1.31 (0.4833–4.00)	0.599
23.8, 334	>42.2, 995	1.99 (0.9654–4.00)	0.062
>334, 670	>42.2, 995	2.27 (1.1019–5.00)	0.026
>670, 2830	>42.2, 995	5.34 (2.5651–11.0)	<0.0001
>2830, 6940	>42.2, 995	1.50 (0.4366–5.00)	0.518
23.8, 334	>995, 3310	4.59 (1.5420–14.0)	0.006
>334, 670	>995, 3310	1.51 (0.7256–3.00)	0.271
>670, 2830	>995, 3310	5.77 (2.4314–14.0)	<0.0001
>2830, 6940	>3310, 1,160,000	1·0 (Reference)	

* ORs adjusted for other variables present in the model.

In contrast to above, the hosts from which a higher number of pathogens were reported were less likely to be associated with an emerging human pathogen outcome. It is interesting to note that whereas the multi-host pathogens are believed to be responsible for the majority of emerging infectious diseases in humans [8,25,40], hosts from which multiple pathogens have been reported do not support this phenomenon. This might be due to enhanced research or study efforts focused on certain host species, but future research might generate more information to explain this apparent contradiction. Statistical interactions indicated that the odds of having an emerging human pathogen status were highest when the host had a higher adult body mass, and the pathogen was able to affect a greater number of host species. It has been reported that >80% of pathogens infecting animals are multi-host pathogens [41].

Statistical interactions indicated that the odds of a pathogen infecting multiple hosts were highest when a host had earlier female maturity >670 to 2830 days and lower (>42.2 to 995 g) birth/hatching weight compared to later (>2830 to 6940) female maturity days and higher (>3.31 to 1160 kg) birth/hatching weight. In addition, smaller animals (< 1 kg body weight) with female maturity within ~2–8 years were more likely to host multi-host pathogens than animals with a body weight of 3.3–1160 kg and attaining female maturity within ~8–19 years. It has been reported that 'fast-lived' mammal species with shorter lifespans are more likely to host zoonotic pathogens [42]. This might hold true for multi-host pathogens also.

The current study has limitations. Host characteristic investigations were limited to four host classes: Amphibia, Aves, Mammalia and Reptilia. Differences at the lower levels of the host classification, such as host Order and Family levels were not captured. Separate analyses of host class data sub-sets are required to provide additional insights. However, using lower Order classifications would reduce statistical power, since data scarcity for specific Orders and Families is expected.

We used rigorous methodology to compile a host-agent characteristics database; however, the information on the host-agent interactions is likely to expand in the near future. Furthermore, the impact of environmental and social parameters (such as climate change, deforestation, change in land use and increase in travel and trade) on disease emergence, zoonosis and multi-host pathogenicity could not be evaluated. In addition, there will be other important host and agent characteristics, the impact of which could not be evaluated.

Nevertheless, we conclude that the current study highlights the importance of many host characteristics in disease emergence, zoonosis and multi-host pathogenicity. Host class, ability to host multi-pathogens, adult body mass, female maturity days and birth/hatching

weight are the noted examples. So rather than simply acknowledging a role for host factors in disease emergence, we provide empirical evidence to give granularity to this concept. Our findings have relevance for preparedness for emerging infections and zoonotic diseases.

Ethical statement

Informed consent for collection of epidemiological data was not required, as these data were already coded and available in the public domain. No identifiable personal information was used in this study.

CRediT authorship contribution statement

Balbir B. Singh: Conceptualization, Data curation, Methodology, Writing – original draft. **Michael P. Ward:** Supervision, Writing – review & editing. **Navneet K. Dhand:** Supervision, Writing – review & editing.

Declaration of Competing Interest

The authors declare no conflicts of interest.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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