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Emergence of Viral Infections through Food Supply Chain: A Review

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Authors' contributions

This work was carried out in collaboration between both authors. Author RM selected the title of review, managed the literature searches, went through it thoroughly and prepared the first draft. Author AI analyzed the draft for typical errors and arranged it according to the journal protocol. Both authors read and approved the final manuscript.

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ABSTRACT

All living organisms may act as host to a wide range of viruses, and can infect the human body causing severe illness or even death. Viruses have often been important in burdening infections and other illnesses and require special attention because of their different behaviour as compared to bacteria. Two highly pathogenic corona-viruses—severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS)—supposed to be emerged from an wet market in china resulted in a global epidemic which took a tool on human lives and currently also the world is fighting a deadliest viral infection caused by a small pathogen possibly transmitted through the food chain in a wet market again in china. The environment is the reservoirs for many of these viruses and any human handling of animals carrying such viruses finds an easy route into human body. Besides, there had been various food borne outbreaks throughout the world due to contaminated agricultural produce, packaging, processed foods or through infected food handlers. Such incidents have prioritized the need for effective control measures, intensified research and risk assessment measures in controlling such outbreaks. This review highlights a brief description of viral transmissions, virus and human gut response and preventable strategies in the food chain to contain such infections.

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1. INTRODUCTION

Generally food selection is based on factors like nutritional needs, taste, religious beliefs and most important the regional availability. Safety in food industry is a recent advancement after recognizing viruses as important causes of food-borne disease. Plants, animals and humans all acts as hosts of the wide range of viruses and their infections get transmitted to human body through several means (Table 1).

Most documented routes of transmission are respiratory route (by droplets), faecal-oral route, sexual route, through vectors or through infected animals (zoonotic). Rapid advancement in geographical movement of people and goods together with global warming have resulted in quick transmission of infectious virus to a wide range of population at the lowest possible time resulting in an outbreak [1]. Food borne viral gastroenteritis is commonly caused by Noroviruses (NoV) and Hepatitis A virus (HAV), can also be transmitted by foodborne routes [2]. Recent evidences show that HIV and Ebola hemorrhagic fever was likely associated with human exposure to blood and body fluids of nonhuman primates hunted and butchered for food in Sub-Saharan Africa. Highly pathogenic viruses, SARS-CoV and MERS-CoV, resulting in severe respiratory syndrome with an initial outbreak of SARS-CoV in Guangdong Province, China was also supposed to be associated with selling of small carnivore, the palm civet in this province. The virus was then found in animals sold in the same Chinese market [3].Whereas, MERS-CoV which emerged in Middle Eastern countries in 2012 and got transmitted through dromedary camels was imported into China [4]. Both these viruses have originated in bats and studies suggest that large number of human corona viruses are carried by different bat species and evidences of interspecies transmission from bats-animals-humans (Fig. 1) further increases the risk of emerging infections because of mutations of these viruses [5].

Table 1. Viruses that are, or have the potential to be, transmitted via food or its handling and their site of infection in the human body

Site of Infection	Virus
Neural tissue and nervous system	Enterovirus, Nipah virus, Poliovirus*, Parechovirus*, Tick-borne encephalitis virus
Respiratory system	HPAI H5N1, SARS , MERS, COVID 19
Liver	HAV HEV
Intestinal system	NoV HRV Sapovirus, Astrovirus, Adenovirus, Aichi virus

*Note: Enteric viruses can also be airborne, blood borne (including vector-borne) or sexually transmitted. **
Source: FAO and WHO 2008. viruses in food: scientific advice to support risk management activities

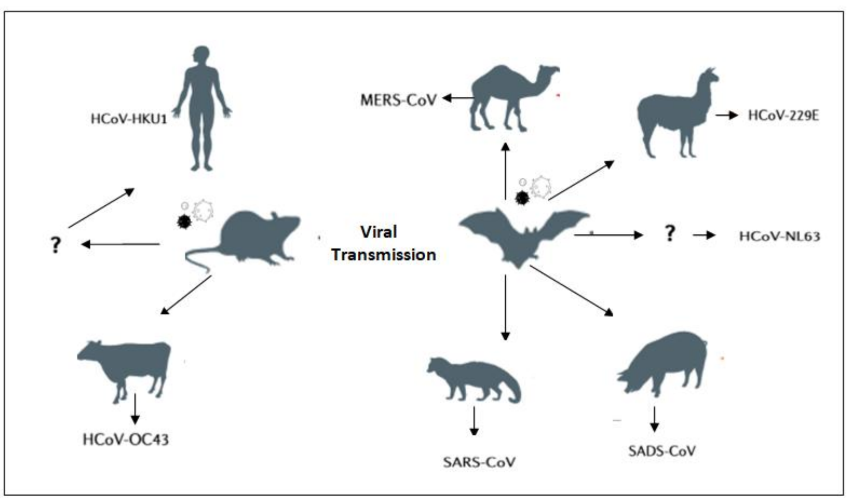

Fig. 1. Interspecies transmission from bats-animals-humans

The origin of SARS-CoV-2 which resulted in current global endemic is still under investigation however; it has one thing in common with SARS that both started in wet food markets of China [6]. The extremely crowded seafood market and constant close exposure of available live and dead animals like bats, pigs, snakes, dogs etc could be a possible reason of transmission of zoonotic diseases from animals to humans.

In this review, we first summarize the primary route of transmission of these viruses resulting in an outbreak, emphasize on human gut microbiome changes once body is exposed to infection and possible preventive strategies required in current food industry and related fields to keep a check on such outbreaks which can pose an international health threat.

2. SUPPLY CHAIN AS A SOURCE OF VIRUSES; FROM FARM TO FORK

The differences in agricultural practices and increased technological advancement among different nations has given rise to import and export of food produce across the globe to make even the perishable items available for human consumption throughout the year. Various products like fresh and preserved fruits, vegetables, meats, poultry and dairy products are extensively traded. The demands are increasing to overcome the nutritional deficiencies, to satisfy human palate and mostly to get commercial gains in food industry. Worldwide, Norovirus (NoV) is the leading agent of acute gastroenteritis, causing about 1 in 5 cases in developed countries [7]. Majority (70%) of these result because of infected food handlers and common foods associated like leafy greens, fresh fruit and shellfish in the form of salads etc [8]. An outbreak of NoV gastroenteritis in Germany in 2012 was reported to be transmitted through frozen strawberries imported from China [9] and increased incidences of HAV in Italy were recorded to be because of frozen berries imported from various European nations [10]. The food borne viral infections usually spread through fecal-oral route; consuming infected foods or from person to person contact. Insufficient agricultural practices have also been found responsible for its spread like use of contaminated irrigation water on agricultural products as route of transmission of virus due to differences in viral survival on different surfaces [11]. Another step in viral transmission in food chain comes at processing level, whether it is handling of different types of animals while slaughtering or carrying out different food storage or processing measures. Virus usually remain stable under refrigeration and freezing with no reduction of MNV (Murine NoV) on certain foods like spinach and spring onions over months of frozen storage and few remain stable even at low pH [12]. The packaging material if infected with any virus also poses a threat by transmitting the same to the food packed in it. Certain control strategies used to keep food microbiologically safe may not be directly applicable to viruses.

Before 2003, corona viruses were not much recognized as human corona viruses resulted only in acquiring cold. With the occurrence of SARS epidemic, coronavirus got much attention as emerging infectious viruses. Its isolation from the lungs of the infected person demonstrated it as previously unrecognized coronavirus [13,14]. Further, the evidence suggest that several corona viruses including SARS-CoV and MERS-CoV were supposed to be transmitted from their original host (Bat) to another mammal by faecal–oral transmission and acquired further mutation before getting into the human body. And studies further predict some strains of bat SARSr- CoV (bW1V1 and bRsSHC014) have ability to cross the species barriers between bats, civets and humans which resulted in the infection [15,5]; a similar scenario which might have happened for MERS- CoV transmission from bats to camels to humans [16,5]. The recently recognized coronavirus SARS-CoV-2 which erupted from a seafood market in Wuhan, China; where both live and on spot slaughtered species of many animals are sold, also presented its infection as deadly with human to human transmission. [6] This virus is also classified as betacoronavirus like other human corona viruses. These evidences related to coronaviruses and their spill over to humans due to varied reasons and presence of such viruses in natural environmental reservoirs increases the possibility of their adaptive mutations and emergence as outbreaks or endemics like SARS-CoV-2.

3. HUMAN GUT MICROBIOTA AND RESPIRATORY VIRAL INFECTIONS

It is a known fact now that gut-microbiota influences immune responses in several diseases there by effecting health. Several studies suggest that changing gut metabolome through different diets have resulted in positive outcomes in viral and lung infections as well. A diet high in fermentable fiber when fed to mice in a study, decreased lung damage and increased survival during influenza virus infection [17]. Similarly, feeding a diet rich in polyunsaturated fatty acid (PUFA) docosahexaenoic acid (DHA) reduced lung inflammation and damage during respiratory syncytial virus (RSV) infection in mice [18]. Weight loss has been commonly observed after any viral infection, most probably due to decreased food intake because of low appetence. It cannot be ignored that the intestinal microbiota interacts with not only the host immune response but also consequently with antiviral immune responses. Studies show that changes in the gut metabolome after RSV infection is observed in lipid metabolism. There is seen an abundant increase of Multiple PUFAs along with anti-inflammatory DHA following RSV infection [19].Whether these have an effect on the resolution needs more studies to prove.

Our life style and food habits can directly influence the dynamics of gut microbiome; thereby increasing the scope of manipulating the gut microbiome to influence the disease occurrences and body's response. With advancement in gut research commensal intestinal bacteria have been shown to modulate human immune system even in diseases [20]. Probiotics in any form, yogurt, cheese or supplements contains immunostimulatory substances which have shown to decrease the severity in upper respiratory tract infection and Norovirus gastroenteritis [21,22]. It is also believed that Vitamin A also has antiviral effects which are activated by *Lactobacillus* genus through production of interferons [23]. Microbiota has also been seen to have an e□ective immune response against the *Vaccinia virus* (VACV), a large and complex enveloped virus [24] and *Influenza A virus*, by stimulating influenza-specific T-cell responses [25]. There is a well established relationship between commensal bacterial, probiotics, immune cells and epithelium mediates antiviral effects of microbiota; enteric cells control increased mucus production and synthesis of reactive O2 species and defensins to curb viral replication [26].

In spite of microbiotal barriers against various viruses, it cannot be ignored that there are certain viruses which enter host, escape the immune response and result in severe infections. Such viruses have evolved with time to interact with the microbiota, use it, and facilitate viral infection [27]. This can be believed to be the reason behind severity of infections due to viruses like SARS CoV, MERS CoV and SARS-CoV-2. These viruses presented cross-species transmission, which means the virus has crossed the different barriers and its epidemiology has reached to a pandemic form from its original host to the infected human. An important perspective in this can be that human and non–human primates present a considerable difference in eating habits, estrus cycle, physical and sexual behaviour, gut microbiota and also the gestation period. So it makes it extremely important to understand all aspects of the barriers crossed by such viruses and their pathways in future research too.

4. PREVENTIVE STRATEGIES IN FOOD INDUSTRIES FOR SAFE CONSUMPTION OF FOOD

Due to increased global trade in food production system, our single meal may comprise of numerous locally and globally produced foods. So the practices and the handlers involved in producing, preparing, packaging and consuming food, links our health with the health of the people globally in both direct and indirect ways. All these factors result in emergence, re-emergence, and spread of food-borne pathogens or other illnesses across the worlds which are otherwise preventable.

4.1 Infection Prevention at Source

Increased global population in several nations like china and India are the potential hotspots for the infections to emerge. Besides, the aged population in developed nations like US, Italy, France and UK are increasingly vulnerable to illness (as reported in SARS-CoV-2 endemic as well), associated with consumption of foods tainted by food-borne pathogens [28] with approximately 75 percent of processed food items containing ingredients from another country [29]. Studies have reported that viruses have become transmissible by the faecal-oral route hence, major control measures are required at source like use of disease free seeds and planting material, proper sewage disposal near and around farms, and hygienic harvest practices. All these measures if strictly taken care off at source will benefit in getting a disease free agricultural product.

Consumption of meat has largely increased in last decade in both developed and developing countries because of popularity of animal protein; which inturn increased the human animals contact and possibility of zoonotic transmission of viruses. The trend of eating exotic animals in certain region has further intensified this transmission; which probably is a threat to human health. In poultry and animal breeding farms, fecal shedding especially of diseased animals has to be controlled and taken care off. And whenever, the animal waste is used for manure making, the pathogens present in it should be inactivated before adding it to soil. Wet markets have been characterized as an important source of emerging infections like SARS CoV and SARS-CoV-2 (6); emergence of proper regulatory laws to maintain hygiene in such markets; separate markets for animal and plant product; training and awareness regarding the health hazards to the handlers who come in contact with the blood and fluids of the animals is of urgent need.

4.2 Infection Prevention during Processing

Usually processing industries focus on control of bacterial contamination in the food products; e□ciency against viruses is a recent concept after severe global outbreaks. Viruses are usually resistant to bacteriological control measures like refrigeration, freezing, pH etc. [30]. The use of mild thermal processes currently by industries to retain flavour of food products may further increase the risk. On the other hand, plant extracts from grape seeds, cranberries, mulberries, black raspberries and pomegranates possessing antiviral properties have shown reduced virus adsorption to cells in case of FCV, MNV and HAV with some viral replication inhibition too. [31,32]. There are also evidences of spice oil a□ecting the capsid and RNA directly [33]. Plant Phenols and flavonoids have also reported to show anti viral properties against rotavirus and FCV [34]. Citric acid has shown antiviral effect against human NoVs and milk proteins may also interfere with virus infection, e.g. lactoferrin blocks rotavirus [35], FCV and PV [36,37] entry into the cell. Despite of effectiveness of the compounds in in-vitro studies, there has been very limited application of these to date because not enough concentrations of these compounds are present in a food. But extraction of these compounds from the plant sources and using them in required concentrations for raw and processed food preservation may increase their scope in controlling the transmission of viruses. There arises a need of reliable tools for validation of virus inactivation in food industry. It is getting inevitable to have a common platform of researchers, industry experts and regulatory bodies to develop new technologies e.g. Next Generation Sequencing, 'omics to viruses.

4.3 End-use Preventive Strategies

At the first place there is a need to include training and compliance of food handlers in practicing regular clinical checkups, vaccination and personal hygiene including effective hand washing at regular intervals. They should be aware about the possible spread of infections through contaminated food and improper handling. Proper guidelines should be prepared and followed by food industries and strict regulations should be enforced by the controlling authorities. Government can make timely use of disinfectants and fumigation as mandatory programmes for food industries. There is also a need for consumer awareness regarding healthy food habits and maintenance of hygiene in and around households. Proper washing of produce with clean water before consumption together with use of clean utensils, forks knives, spoons on daily basis to stop bacterial growth. For general public awareness food and nutrition boards can prepare a list of foods most susceptible to carry viruses and which in past have resulted in various outbreaks. Implementing consumer-friendly guidelines based on sound science to ensure that foods do not become contaminated during end use is important. Such awareness programmes can also be carried out through print, audio visual and social media to create a safe food culture.

5. WHAT WE CAN DO IN CURRENT SITUATION

As stated by health workers dealing with SARS-CoV-2 patients, most infected people show mild respiratory symptoms where as elderly and people with underlying health causes like diabetes, cardiovascular disorders, obesity, hypertension or cancer possess higher risk of developing serious illness due to infection or even death [38]. The possible reason could be the weak immune system of elderly in general and in those with underlying diseases; because their body is already fighting other disorders. Besides maintaining good hygiene and frequent hand washing, our bodies need right type of foods to boost its immune system. High intakes of carbohydrates and some fats not only leads to obesity but are also supposed to suppress immune system. Good quality proteins are always important for body's defence mechanism.

Adding generous amount of fruits and vegetables in our daily diet increases our intake of antiviral and antibacterial substances. Besides it is always better to drink plenty of fluids to keep our body and our immune cells hydrated. Not to be malnourished is also important to combat any illness. Elderly or those battling certain illnesses are at higher risk of getting malnourished as well as infections besides taking longer time for recoveries. Hence, a focus on balanced amount of foods rich in carotenes, vitamin C and D, Zinc, proteins together with probiotics, adequate sleep and stress management will help immensely in making our immune system healthy. For those under self-isolation with symptoms, it becomes very important to maintain optimum nutrition and proper hydration even if the appetite is low. Avoiding consumption of processed foods and taking comfort foods is beneficial for mental health. Quit smoking if you are a smoker, exercise regularly, maintain proper hygiene, sleep well and minimise stress.

6. CONCLUSION

The previous outbreaks of all viral infections whether food borne or those spreading through food chain especially SARS CoV and MERS CoV, illustrated the need for better and clear communication between public health community, researchers, industries and governments. E□ective tools and technologies to ensure control of viruses in the food chain, can significantly reduce their infections. While the time of outbreak is impossible to predict, going by the previous experience and the knowledge about presence of reservoirs of viruses is calling for an effective response, prompt action and timely development and implementation of effective counter measures and disciplined lifestyle. The emergence of another outbreak (SARS-CoV-2) by a virus from the same family which resulted in previous outbreaks emphasizes the perpetual challenge of emerging infectious diseases and the importance of global preparedness.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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