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The imported infections among foreign travelers in China: an observational study

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Abstract

Background: In the past few decades, globalization has rendered more frequent and intensive population movement between countries, which has changed the original disease spectrum and brought a huge health impact on the global population including China. This study aims to describe the spectrum and epidemiological characteristics of imported infections among foreign travelers travelling to China.

Methods: The data on imported infections among foreign travelers were obtained from Custom Inbound Screening System (CISS) and the National Notifiable Infectious Disease Reporting System (NNIDRS). All the infections were classified into respiratory, gastrointestinal, vector-borne, blood/sex-transmitted and mucocutaneous diseases, of which case numbers and incidences were calculated and the proportions were compared among subgroups.

Results: In total, 17,189 travelers diagnosed with 58 imported infectious diseases were reported from 2014 to 2018, with an overall incidence of 122.59 per million. Respiratory infection (7,351 cases, mainly influenza) and blood/sex-transmitted diseases (6,114 cases mainly Hepatitis B and HIV infection) were the most frequently diagnosed diseases, followed by vector-borne infections (3,128 cases, mainly dengue fever and malaria). The highest case number was from Asia and Europe, while the highest incidence rate was from Africa (296.00 per million). When specific diagnosis was compared, both the highest absolute case number and incidence were observed for influenza. An obvious seasonal pattern was observed for vector-borne diseases, with the annual epidemic spanning from July to November. The origin–destination matrices disclosed the movement of imported infection followed specific routes.

Conclusions: Our study provided a profile of infectious diseases among foreign travelers travelling to China and pinpointed the target regions, seasons and populations for prevention and control, to attain an informed control of imported infections in China.

Keywords: Globalization, Imported infectious diseases, Public health impact, Epidemiological characteristics, China

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Introduction

Before the COVID-19 epidemic, international travel had persistently increased in frequency driven by globalization, with the imported infectious diseases causing an increasingly serious public health concern faced by almost all countries. Foreign travelers or immigrants account for a high proportion of all travelers, with a critical risk of spreading the diseases across borders by which pathogens can reach new human populations or animal communities. Particularly for the vector-borne disease, the movement of patients beyond endemic countries has



threatened long-term eradication goals, such as malaria [1]. Moreover, the imported cases continue to pose challenges for diagnosis and management for physicians in non-endemic areas, where it can be difficult to treat and result in high mortality. Health care providers need a complete understanding of the spectrum of imported infectious diseases and their epidemic patterns, which is critical in containing the potential epidemic or pandemic caused by imported diseases.

In China, the number of foreign travelers has steadily increased from 83.44 million person-times in 2000 to 141.20 million person-times in 2018, associated with increased reports of imported infections from 5,261 cases in 2014 to 10,157 in 2016 and 14,700 in 2018 [2, 3]. The imported infection was mainly captured by the costume entrance quarantine and national surveillance system on travel related disease [2–4], which had provided valuable information about the composition, and trends of imported infections. However, infection spectrum and the time when travel-related infection was present among foreign travelers were significantly different with other arriving travelers [2, 3], and the specific infection spectrum and epidemiological characteristics of them remained unclear, which might impede their timely and accurate diagnosis, treatment and management, especially those infections that are not endemic or rare in China. In the current study, we focused on infection diagnosed from the foreign travelers (here referred to as those with foreign citizenship) to describe the pathogen spectrum and their related epidemiological features, and explore their potential impacts on public health.

Material and methods

Data collection

Full details of obtaining the data on international imported infections had been provided in a previous study [4]. Briefly, data were extracted from two anonymous and delinked databases: the Custom Inbound Screening System (CISS) that had covered all 272 entry-exit ports in China (Figure S1), and the National Notifiable Infectious Disease Reporting System (NNIDRS) of Chinese Center for Diseases Control and Prevention (CDC) which covered all 31 provinces in the mainland of China. The data extraction process and the criteria of inclusion and exclusion were shown in Figure S2. For diagnosis of a specific disease, SOP released by the General Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China (AQSIQ) was followed that covered all processes of sample collection and laboratory tests (Figure S3) [2]. For the screened patients, a standard questionnaire interview was applied to record the clinical and epidemiological data that were related

to the travel illness (Figure S4). A predefined standard dataset was used to extract the data from the patient's medical records, including the travel related epidemiological information, and clinical data that supported the diagnosis. For the purpose of calculating the incidence rate, the inbound arrivals data in the mainland of China were obtained from the Annual Report of China Tourism Statistics (ARCTS) 2015 to 2019. The yearly and monthly numbers of foreign travelers from 2014 to 2018 were calculated for six continents and 23 selected countries with available data about foreign travelers in the ARCTS.

Definitions and classifications of imported infections

Altogether 67 infectious diseases were screened from two reporting systems, based on which five syndromic diseases were classified, including respiratory, gastrointestinal, vector-borne disease, blood/sex-transmitted disease and mucocutaneous disease as previously described [2].

Six possible travel purpose were designed and used in this analysis: tourism; labour, business; research or student; visiting friends and relatives, etc. Travelers were grouped into six geographic areas according to their originating regions: Africa, Asia, Europe, Latin America, North America, and Oceania.

Statistical analysis

Descriptive statistics were performed for all variables. Continuous variables were summarized as median and range. Proportions were calculated regarding various disease categories, which were compared for the difference among subgroups by Chi-square test. The `chisq.test` function in the stats package in R was used to implement subgroup comparisons. Incidence rates were calculated as the case number divided by the total number of arriving foreign travelers. We standardized the incidence rate by inbound travel number for each infectious disease, determined the percentage rank, and further represented data as thermodynamic diagrams as previously described [5, 6].

For each reported infectious disease, we aggregated the annual mean case number exported to each province by the source countries/continents, and further constructed origin–destination matrices. The SAS software (version 9.4) was used for data extraction, sorting and cleaning. The R project (version 3.6.3) and relevant packages (such as `dplyr`, `arsenal` and `ggplot2`, etc.) were applied to analyze the data, prepare the tables and draw heatmaps and percentage bar plots [7–9]. ArcGIS software (version 10.5) were used for graphics presentation.

Results

Demographic characteristics and infection types of the imported diseases

During 2014–2018, a total of 17,189 travelers with 58 imported infectious diseases were confirmed out of totally 140,210.30 thousand person-times foreign travelers, with an overall incidence of 122.59 per million, which comprised of 14,452 cases reported from CISS and 2,737 reported from NNIDRS (Figure S2). Travelers of male gender, aged 15–44 years, those originating from Asian countries have accounted for a higher proportion of travel related cases than their counterparts (all $p < 0.001$) (Table 1).

The respiratory infection (RI) had the highest average incidence of 24.96 per million and showed ascending tendency over the 5 study years (Fig. 1A). Influenza was most frequently seen among all types of respiratory diseases determined from the travelers, with an extraordinarily high level in the year 2017 and 2018 (Fig. 1B). Blood/sex-transmitted infection (BSTI) was the second most frequent disease with a consistently increasing incidence from 18.10 per million in 2014 to 70.13 per million

in 2018. HIV infection, syphilis, hepatitis B and hepatitis C were among the most frequent diagnosis, with incidence rates of 14.12, 5.89, 18.92 and 4.48 per million, respectively (Fig. 1B). When data from two reporting systems were separately analyzed, respiratory infection and vector-borne diseases were the most common syndrome classification from CISS and NNIDRS, respectively (Figure S5).

The spectrum of imported infection

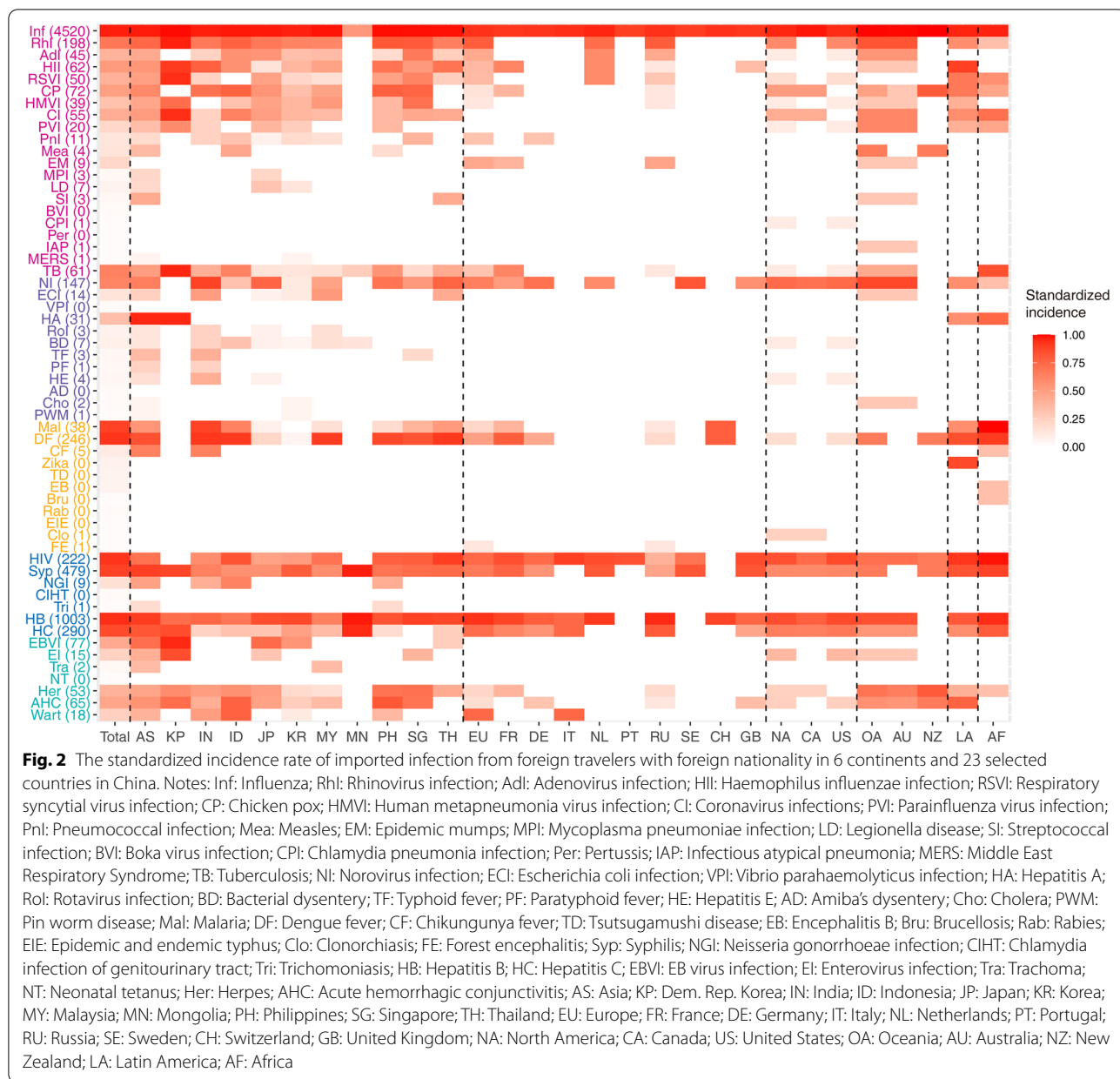
Totally 58 imported infectious diseases were diagnosed among 17,189 travelers (Fig. 2). The 10 most common infections were influenza (with a proportion of 36.96%), followed by hepatitis B (15.43%), dengue fever (13.09%), HIV (11.51%), malaria (4.86%), syphilis (4.81%), hepatitis C (3.66%), rhinovirus infection (1.33%), and tuberculosis (1.07%), and norovirus infection (1.01%), which collectively had taken 93.72% (16,110/17,189) of the confirmed diagnosis. Their annual incidence kept increasing during the study period, especially for HIV infection, hepatitis B and norovirus infection (Fig. 3A).

Table 1 The characteristics of imported cases among foreign travelers in Chinese mainland, 2014–2018

	Overall (n = 17,189)	Respiratory (n = 7351)	Gastrointestinal (n = 282)	VBD (n = 3128)	BSTI (n = 6114)	Mucocutaneous (n = 314)	p value
Sex							<0.001 ^a
Male	12,347 (71.8)	5769 (78.5)	165 (58.5)	1861 (59.5)	4310 (70.5)	242 (77.1)	
Female	4842 (28.2)	1582 (21.5)	117 (41.5)	1267 (40.5)	1804 (29.5)	72 (22.9)	
Age	33 (25–45)	35 (25–48)	31 (23–51)	29 (20–41)	33 (26–42)	34 (25–46)	<0.001 ^a
0–14	1485 (8.6)	932 (12.7)	30 (10.6)	469 (15.0)	18 (0.3)	36 (11.5)	
15–29	5326 (31.0)	1755 (23.9)	97 (34.4)	1130 (36.1)	2258 (36.9)	86 (27.4)	
30–44	6040 (35.1)	2425 (33.0)	68 (24.1)	903 (28.9)	2540 (41.5)	104 (33.1)	
45–59	3172 (18.5)	1558 (21.2)	33 (11.7)	472 (15.1)	1050 (17.2)	59 (18.8)	
≥ 60	1166 (6.8)	681 (9.3)	54 (19.1)	154 (4.9)	248 (4.1)	29 (9.2)	
Destination							<0.001 ^a
Africa	907 (5.3)	137 (1.9)	8 (2.8)	479 (15.3)	282 (4.6)	1 (0.3)	
Asia	10,105 (58.8)	4833 (65.7)	188 (66.7)	2545 (81.4)	2278 (37.3)	261 (83.1)	
Europe	1342 (7.8)	694 (9.4)	21 (7.4)	22 (0.7)	594 (9.7)	11 (3.5)	
Latin America & Caribbean	165 (1.0)	94 (1.3)	4 (1.4)	19 (0.6)	42 (0.7)	6 (1.9)	
North America	722 (4.2)	520 (7.1)	34 (12.1)	3 (0.1)	157 (2.6)	8 (2.5)	
Oceania	536 (3.1)	468 (6.4)	19 (6.7)	10 (0.3)	26 (0.4)	13 (4.1)	
unknown	3412 (19.8)	605 (8.2)	8 (2.8)	50 (1.6)	2735 (44.7)	14 (4.5)	
Infection year							<0.001 ^a
2014	1280 (7.4)	445 (6.1)	10 (3.5)	334 (10.7)	477 (7.8)	14 (4.5)	
2015	2413 (14.0)	1025 (13.9)	16 (5.7)	644 (20.6)	693 (11.3)	35 (11.1)	
2016	3545 (20.6)	1740 (23.7)	63 (22.3)	494 (15.8)	1177 (19.3)	71 (22.6)	
2017	5421 (31.5)	2351 (32.0)	69 (24.5)	1254 (40.1)	1625 (26.6)	122 (38.9)	
2018	4530 (26.4)	1790 (24.4)	124 (44.0)	402 (12.9)	2142 (35.0)	72 (22.9)	

VBD Vector-borne disease, BSTI Blood/sex- transmitted infection

^a Test for the categorical variable by Chi-square test



(See figure on next page.)

Fig. 3 The spectrum of imported infections in foreign travelers with foreign nationality in the mainland of China, 2014–2018. **A** The annual incidence rate of 58 imported infectious diseases. **B** Sex, age, and original continent distribution of 58 different imported infections. Notes: Inf: Influenza; Rhl: Rhinovirus infection; Adl: Adenovirus infection; Hll: Haemophilus influenzae infection; RSVI: Respiratory syncytial virus infection; CP: Chicken pox; HMVI: Human metapneumonia virus infection; CI: Coronavirus infections; PVI: Parainfluenza virus infection; Pnl: Pneumococcal infection; Mea: Measles; EM: Epidemic mumps; MPI: Mycoplasma pneumoniae infection; LD: Legionella disease; Sl: Streptococcal infection; BVI: Boka virus infection; CPI: Chlamydia pneumonia infection; Per: Pertussis; IAP: Infectious atypical pneumonia; MERS: Middle East Respiratory Syndrome; TB: Tuberculosis; NI: Norovirus infection; ECI: Escherichia coli infection; VPI: Vibrio parahaemolyticus infection; HA: Hepatitis A; Rol: Rotavirus infection; BD: Bacterial dysentery; TF: Typhoid fever; PF: Paratyphoid fever; HE: Hepatitis E; AD: Amiba's dysentery; Cho: Cholera; PWM: Pin worm disease; Mal: Malaria; DF: Dengue fever; CF: Chikungunya fever; TD: Tsutsugamushi disease; EB: Encephalitis B; Bru: Brucellosis; Rab: Rabies; EIE: Epidemic and endemic typhus; Clo: Clonorchiasis; FE: Forest encephalitis; Syp: Syphilis; NGI: Neisseria gonorrhoeae infection; CIHT: Chlamydia infection of genitourinary tract; Tri: Trichomoniasis; HB: Hepatitis B; HC: Hepatitis C; EBVI: EB virus infection; El: Enterovirus infection; Tra: Trachoma; NT: Neonatal tetanus; Her: Herpes; AHC: Acute hemorrhagic conjunctivitis

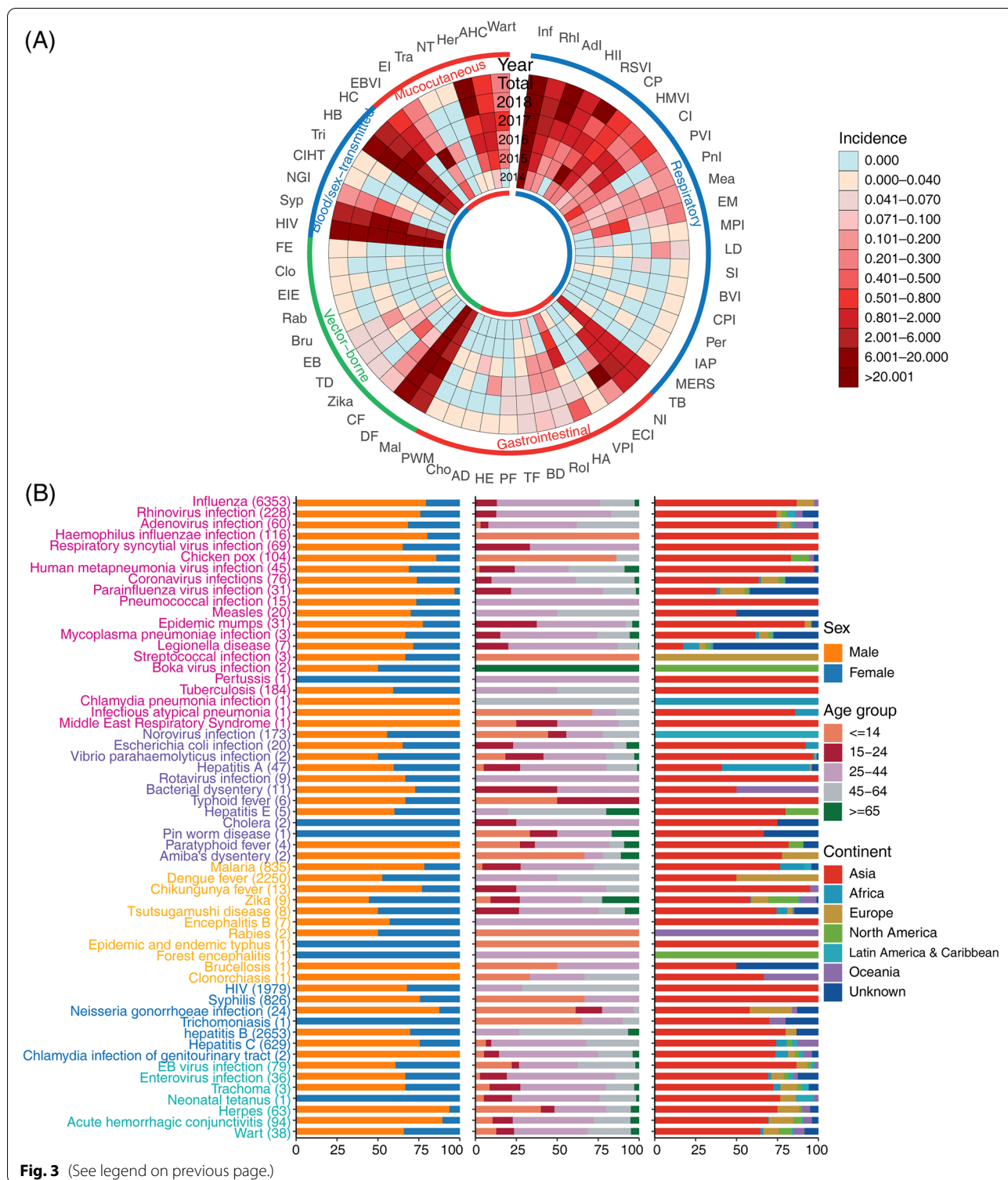
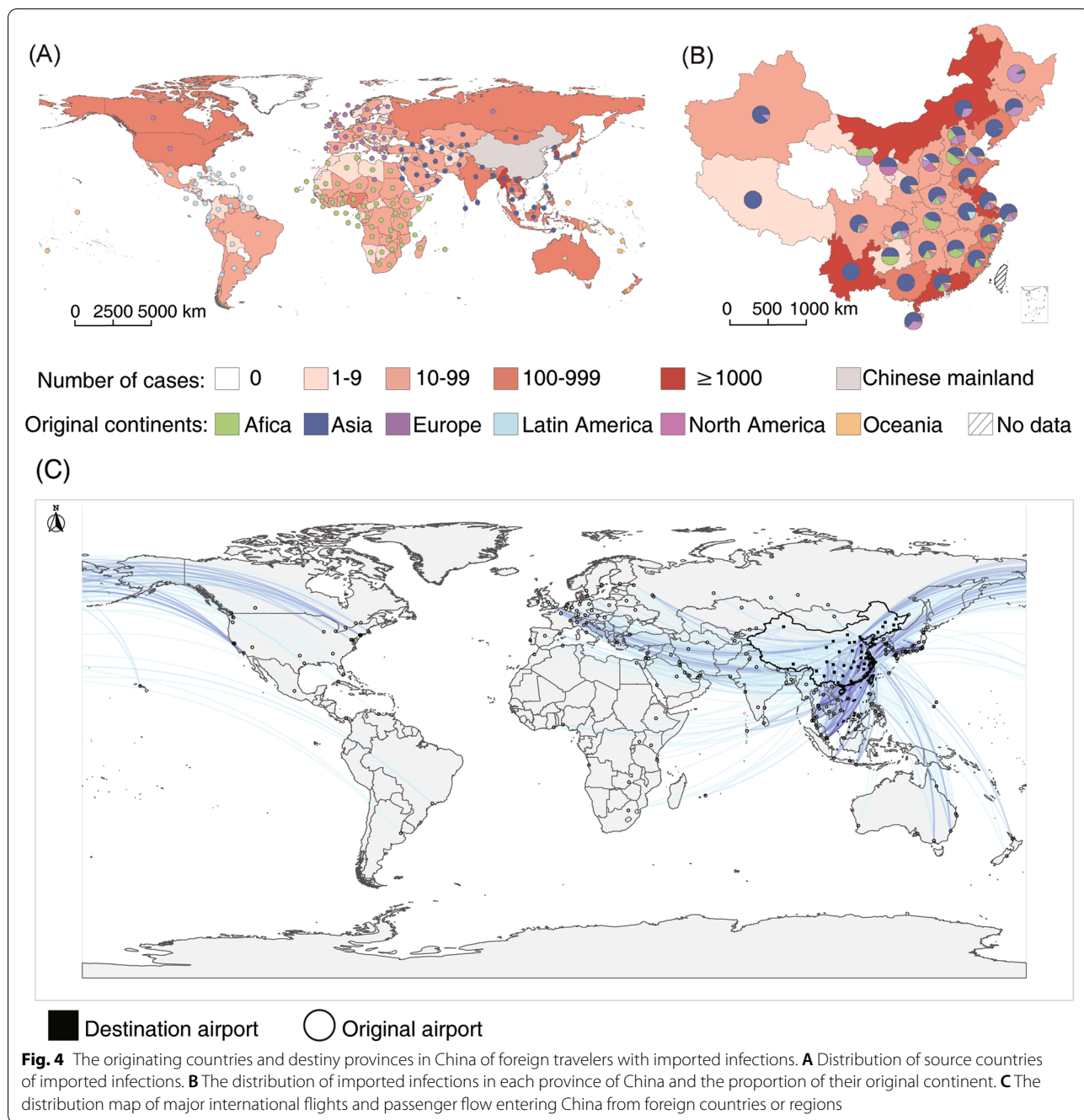


Fig. 3 (See legend on previous page.)

travelers had taken the predominant part, accounting for 59.02% (10,105/17120) of all imported cases, followed by those from European and African countries. Within Asian countries, Korean travelers had contributed the

highest number of cases with RIs, BSTIs and VBDs. The destination provinces which had reported more than 1000 imported cases included Yunnan (3,134 cases),



Guangdong (2,017 cases), Shanghai (1,939 cases), Inner Mongolia (1,447 cases) and Jiangsu (1,348 cases).

The major international flights and traveler inflow from foreign countries or regions were mapped (Fig. 4C). In 2016, the annual traveler flow from foreign international airports to Chinese airports was about 77.09 million. Among them, the continent with the largest annual inflow number of international flights to China is Asia (62.80 million), followed by North America (5.62

million), Europe (5.60 million), Oceania (1.80 million), Africa (1.00 million), and Latin America (0.27 million). The movement of imported infection followed specific routes (Fig. 4), in that the connections were more frequently seen between African and Hubei, Guizhou and Jiangxi province (13 cases on average per year), and between Asian (mainly including Burma, Vietnam and Laos) and Yunnan province (592 cases on average per year,) and between Asian (Mongolia and Russia) and

Inner Mongolia (233 cases on average per year). Notably, the imported patients travelling to metropolises such as Beijing, Shanghai and Guangdong Provinces tended to be multi-continental sources (Fig. 4B and C). The annual travelling data were available from six continents and 23 countries, which were used as denominator for estimation of incidence. This had accounted for 79.25% (111.12/140.21 million person-times) of total travelling population and 45.96% (7,900/17,189) of total imported cases. When related to the source regions, the highest case incidence was reported from the African travelers (296.00 per million), in contrast with the highest case number from Asia, while the lowest incidence was reported from European countries (41.70 per million). When specific diagnosis was compared, both the absolute case number and incidence rate was observed for influenza (Fig. 2).

Discussion

Globalization has promoted the growth of population movements between countries, which has changed the global disease spectrum and brought a huge impact on the public health. In China, imported infectious diseases remain the major cause of morbidity and mortality, partially owing to the close connection of China with the rest of the world through travel and trade. The previous publications that were built on the real-time monitoring system from the enter-exit port have provided a snapshot of travel related infection over a geographic area, or time frame, however, not differentiate between native citizens and foreigner travelers for their role in spreading the imported infectious diseases.

In this study, rather than study all international travelers, we focused on the foreign travelers for analysis, comparing the imported diseases by their travel related data to identify countries, seasons and travel modes that were associated with a high incidence of imported infections. We determined that Asian travelers contributed the highest number of incoming travelers and cases with imported infectious diseases probably due to the geographical proximity and frequent international exchanges. In contrast, African travelers had the highest incidence of imported infection, thus posing as the high priority in inbound quarantine. The imported patients were primarily originated from bordering countries of China, with a high possibility of causing local epidemics [10], such as importation of dengue from Vietnam, Laos and Myanmar into Yunnan, and blood/sex-transmitted diseases from Mongolia and Russia into Inner Mongolia, respectively. In contrast, the imported patients reported in metropolises or provinces such as Beijing, Shanghai and Guangdong Provinces tended to from a wide range

of source countries, due to a highly complicated transportation exchange around the world.

The spectrum of imported infectious diseases from foreign travelers also varied depending on the travel season and the travel purposes. Except for vector-borne diseases that were extraordinarily overrepresented between July and November, all other infectious diseases were evenly detected throughout the year, posing a persistent burden to the medical quarantine work. The major epidemic peak of VBD in travelers might reflect the epidemic pattern of the disease in the original endemic areas. For example, the peaking season of VBD in southeast Asia spanned from June to September, which coincided with those of the imported VBD [11, 12]. In the case of most important VBDs, dengue disease generally peaked in June and September in Southeast Asian countries [11, 12] while malaria cases generally peaked in September to November in African countries [13], which might be responsible for the high and sustained epidemic peak of imported VBDs from July to November. Previous reports on the imported malaria in the UK [14], Finland [15] and Bulgaria [16], and the imported dengue in Japan [17], Spain [18] and East London [19], had revealed similar epidemic patterns as in the current study. Travelers to dengue-/malaria-endemic countries appear to serve as reliable “sentinels” that may inform the international community of the onset of epidemic activity in specific areas.

During the study period, the incidence of imported infections from foreign travelers had been increasing, especially for gastrointestinal and blood/sex-transmitted diseases. In agreement with the previous report that analyzed all the native and foreign cases [2], respiratory infections were the most frequent diagnosis among five infection types. In addition to the most common diseases including influenza and rhinovirus infections, the diseases with a small number of imported cases but with epidemic potential and risk of high mortality among humans should be given prioritized attention, such as MERS [20]. Notably, the majority of VBDs were identified by the NNIDS instead of through the custom screening, likely due to the relatively long incubation period of most VBD, which was consistent with a previous study [3], indicating the necessity to inquiry recent travel history of suspected foreign cases after their international travel that is helpful for timely and accurate diagnosis, treatment and management of them. Although malaria is no longer endemic in China, the large number and continuous import of malaria have brought great challenges to the goal of a national malaria elimination by 2020 [21]. Emerging imported diseases in recent years such as zika and chikungunya also posed serious threats to human health, therefore

enhanced screening among foreign travelers should be stressed in the high risky population and seasons as we have determined in the current research. In addition, specific disease surveillance and pathogen detection need to be strengthened according to the origin of foreign travelers. For example, it is necessary to strengthen the surveillance of vector-borne pathogens among passengers from Africa, as well as influenza and other respiratory diseases among passengers from European and American countries.

Our study was subject to several limitations. First, the incidence rate might be underreported for most imported infectious diseases because many patients suffering from post-travel symptoms might be missed from the inbound screening, and not seek medical care due to mild symptoms thereafter, or even if they go to the doctor, they were not judged as travel-related illnesses. Second, we could not calculate the incidence rate of foreign travelers regarding their age, sex or original country since the detailed denominator data were inaccessible. Third, the specific location of the infection was difficult to determine for those travelers who have visited several countries before entering China (We used the most recent country they visited as the original country). For example, the imported dengue or malaria cases from France, Germany, or Switzerland, where no endemic diseases exist, were quite suspicious.

Conclusions

In conclusion, our study gave a profile of imported infectious diseases among foreign travelers to China, and pinpointed the target regions, seasons, populations for imported disease prevention and control, which might assist in making medical risk assessments and identifying imported cases, especially those of highly communicable and highly lethal infections. The findings from the current study might also shed light on the prevention and control of imported infection in other countries in the world.

Abbreviations

HIV: Human Immunodeficiency Virus; TB: Tuberculosis; MERS: Middle East Respiratory Syndrome; ITHC: International Travel Healthcare Center; NNIDRS: National Notifiable Infectious Disease Reporting System; CCDC: Chinese Center for Diseases Control and Prevention; COVID-19: Coronavirus disease 2019.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12992-022-00893-7>.

Additional file 1: Figure S1. The distribution of all 272 entry-exit ports in Chinese mainland. **Figure S2.** The flow chart on the data extraction

process and criteria of imported infections in mainland of China, 2014–2018. **Figure S3.** The classification of infectious diseases at ports of Chinese mainland. **Figure S4.** Report card of infectious diseases of the People's Republic of China. **Figure S5.** The disease spectrum of during-travel infectious diseases (A) and post-travel infectious diseases (B) in relation with the inbound provinces in Chinese mainland China, 2014–2018. **Table S1.** The travel reason for during-travel cases of five type of diseases in Chinese mainland, 2014–2018.

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Authors' contributions

W.L., L.-Q.F., and X.-H.G. designed the study. Q.X., Z.-W.L., X.-A.Z., M.-Y.L., J.-L.W., H.-Y.Z., and L.-P.W. performed the literature review, data collection and integration. Q.X., Z.-W.L., X.-A.Z., and M.-Y.L., J.-L.W. conducted the analyses under supervision of W.L., L.-Q.F., X.-H.G., H.-Y.Z., and L.-P.W. helped with the analyses. W.L., L.-Q.F., and X.-H.G. wrote the draft of the manuscript. All authors contributed to and approved the final version of the manuscript.

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Availability of data and materials

Raw data are not publicly available and are protected due to data privacy laws, which were used under license for the current study, but are available upon reasonable request to the corresponding author. The request will be responded within one week.

Declarations

Ethics approval and consent to participate

Not applicable. All patient data were anonymized. This study constituted public health surveillance rather than research in human beings, so ethical approval and consent to participate were not required.

Consent for publication

Not applicable. This study does not contain data from any individual person.

Competing interests

We declare no competing interests.

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