Vincenza Gianfredi^{1,2*}, Daniele Nucci^{3*}, Flavia Pennisi¹, Sandro Provenzano⁴, Pietro Ferrara^{5,6} and Omar Enzo Santangelo⁷

*These Authors equally contributed to the manuscript

¹Scuola di Medicina e Chirurgia, Università degli Studi Vita-Salute San Raffaele, Milan, Italy

²CAPHRI Care and Public Health Research Institute, Maastricht University, Maastricht, The Netherlands

³Servizio di Dietetica e Nutrizione Clinica, IRCCS Istituto Oncologico Veneto, Padua, Italy

⁴Azienda Sanitaria Provinciale di Trapani (ASP Trapani), Trapani, Italy

⁵Centro di Studio e Ricerca sulla Sanità Pubblica, Università degli Studi di Milano-Bicocca, Monza, Italy ⁶IRCCS MultiMedica, Sesto San Giovanni, Milan, Italy

⁷Azienda Socio Sanitaria Territoriale di Lodi (ASST Lodi), Lodi, Italy

Abstract

Background. Zika virus (ZIKV) is an arthropod-borne virus transmitted through infected mosquitos. The aim of this Italian nation-wide study was to evaluate general population's knowledge and attitudes towards ZIKV, its transmission, and travel-related preventive measures.

Methods. This cross-sectional study was conducted between July and August 2017, through a validated questionnaire. Predictors of knowledge were analysed through multivariate regression.

Results. Among 1119 respondents, 20% and 71% knew etiological agent and transmission route of ZIKV infection, respectively. Approximately 43% ignored the preventive measures to be taken after returning from endemic areas. At multivariate analysis, predictors of poor knowledge were age, living in Central or South Italy and Islands, being poorly educated, having never heard of or attended a travel clinic.

Conclusions. This study captures an overall poor knowledge of Zika among general public. This research highlights the need of designing and implementing measures to improve travellers' awareness and protection against ZIKV.

INTRODUCTION

Recently, a series of emerging and re-emerging infectious diseases have constituted major public health challenges globally, with a major impact of Severe Acute Respiratory Syndrome (SARS) [1], Middle East Respiratory Syndrome (MERS), Ebola virus disease (EVD), Malaria, the Zika virus (ZIKV) infection and, lately, the novel Coronavirus Disease 2019 (COVID-19) [2]. Although firstly described in limited specific geographical areas (for instance, MERS-Coronavirus infection in middle-Eastern countries, ZIKV in South America, and EVD in the Western Africa), they have quickly spread worldwide, due to globalization, migration, and the creation of conditions for the smooth travelling of people (e.g., decrease in transport fares, packaged holidays, easier backpacking) [3-5].

Among all, one of the most impacting diseases – af-

ter the challenge posed by SARS-CoV-2 [6, 7] -, is the infection due to ZIKV. This is an arthropod-borne virus (arbovirus) of the family Flaviviridae, genus Flavivirus, which was firstly isolated in sentinel rhesus macaque in the Zika forest of Uganda in 1947 [8]. Although mosquito vectors represent the main route of transmission (primarily Aedes spp, like A. aegypti), post-transfusion, sexual, maternal-to-foetus and intrapartum transmissions have been described [9, 10]. In fact, ZIKV genome has been isolated in saliva, blood, cerebrospinal fluid, urine, breast milk, and amniotic fluid, being ZIKV also responsible for congenital infections and malformations (e.g., microcephaly, cerebral calcifications, severe brain malformations including Guillain-Barre syndrome), and other birth defects [11]. Indeed, from a public health perspective, the great interest on ZIKV is not solely associated with the spread of the infection,

- Key words
- arthropod-borne viruses
- flavivirus
- travel medicine
- tropical disease
- Zika

but mostly attributable to severe congenital malformations in new-borns.

For this reasons, when ZIKV caused an important outbreak in early 2016, started in Brazil and then crossed different international borders, mainly in the Americas [12], the World Health Organization (WHO) Emergency Committee declared it an international public health emergency [13]. This action severely impacted on travelling and travel medicine at that time, during which Brazil was preparing to host the 2016 Olympic Games, with more than 200 nations, 10,000 athletes [14, 15], and hundreds of thousands of tourists from all over the world [16]. Despite the whole situation and the several recommendations (advising, in particular, pregnant women and those planning a pregnancy, athletes, and general public) issued by the WHO [17, 18], the real risk of transmission of ZIKV was valued to be low, since the Olympic Games were held during the winter months, when the distribution of mosquitoes was expected to be low [19]. Moreover, extensive use of insecticides eradicated mosquito population and, most importantly, athletes, trainers and visitors were instructed to use individual protection (wearing appropriate clothing with skin coverage, sleeping under mosquito nets, using contact insecticides for clothing and mosquito nets, and applying insect repellents on a regular basis). Despite all these precautions, many imported cases were registered in several European countries, including Italy [20]. Here, sexual secondary autochthonous cases have been also reported in recent years [21]. Eventually, even though no autochthonous cases of Zika transmission have been notified in Europe and the vast majority of mosquito populations endemic in Italy have proved to be less or not suitable for ZIKV (compared to A aegypti), the identification of mosquitoes belonging to the Aedes spp. (such as A. albopictus, A. koreicus and A. japonicus) in certain areas of the country has raised concerns regarding the possibility of their colonization by ZIKV and a consequent virtual autochthonous spread of the disease [22, 23].

Considering the above, the aim of this nation-wide study was to evaluate the general population's knowledge and attitudes towards prevention of Zika in Italy. The final goal was to detect possible drivers of the compliance towards preventive measures in the general population, as well as identify critical educational needs, useful for developing new methods of empowerment of general public and containing the future transmission of the disease, especially considering the expected high number of travellers to Middle Est for the upcoming 2022 FIFA World Cup in Qatar, which harbours *A. aegypti* mosquito [24].

METHODS

Study design

This cross-sectional study was conducted between July and August 2017, assessing knowledge and attitudes toward ZIKV, its transmission, and the preventive measures by means of modified version of a validated Italian-38-item questionnaire available in literature [25]. This was shortened in order to make the questionnaire easier and to increase the total number of respondents. The new version of the survey was re-validated, and the validation process consisted of the administration of the full questionnaire to 28 adult subjects (not included in the final analysis), to gauge feedback on the overall consistency, reliability, and acceptability in terms of clarity and question formats. The final version of the survey was included in the Supplementary material, available online (*Appendix 1*).

The questionnaire was administered twice, two weeks apart, in order to obtain knowledge and attitude measurements both representative and stable over time. We assessed the test-retest reliability and internal consistency of the questionnaire using the Cronbach's α . It is a measure of how a set of items are related as a group [26]. Higher is the Cronbach's α value higher is the intercorrelations among tested items. A value α greater than 0.70 is generally considered as the minimum acceptable cut-off [27]. Initial Cronbach's α was <0.70; thus, in order to achieve a satisfactory value, surveys' items were iteratively eliminated until an acceptable value was reached. The final, simplified version of the questionnaire included eight items, with a α of 0.81, together with the socio-demographic questions (Table S1, available online as Supplementary material). Overall test-retest concordance was 0.86, ranging from 0.76 to 0.94 according to each item (Table S2, Supplementary material). The validation process took place between January and February 2017.

The new version of the questionnaire was based on a total of 15 items: the first seven investigated socio-demographic characteristics (sex, age, citizenship, area of residency, education, occupation, and partner status), the remaining eight were about the knowledge on ZIKV aetiology, transmission route, preventive measures, and attitude about consultation of travel medicine clinic before travelling abroad. The questionnaire was administered on-line and developed via Google forms®, a userfriendly and free tool used to create survey and collect data. All subjects were voluntary enrolled and questions collected anonymously and no personally identifiable information (as for instance name, and date of birth) were required and stored. Participants were invited trough social networks and no inclusion/exclusion criteria were set, establishing a convenient and purposive sample of general population. All data were stored electronically in a database protected by password, known only to the data manager.

Ethical approval

Ethical approval was given by the local Ethics Committee of the University of Perugia (Comitato Universitario di Bioetica), reference number 2016-09R.

Variables and statistical analysis

Descriptive statistics included counts (percentages, %) for categorical data and mean (and standard deviation, SD) for continuous variables, Since the main endpoint of the study was the assessment of knowledge and attitude of the general population towards ZIKV, these two were assessed as a binary variable, since only one of the possible responses was correct. Specific scores from the survey responses were created and medians used as a cut-off point. Participants with scores equal or below the median were classified as very knowledgeable. The Italian region of residence of respondents categorized into: "South Italy and Islands" (Sicily, Sardinia, Calabria, Basilicata, Apulia, Campania, Molise, Abruzzo), "Central Italy" (Toscana, Umbria, Lazio, Marche) and "Northern Italy" (Lombardy, Piedmont, Liguria, Veneto, Emilia-Romagna, Aosta Valley, Trentino-Alto Adige, Friuli-Venezia Giulia) according to the territorial division of the National Institute of Statistics (ISTAT, www. istat.it).

For the purpose of the multivariate analysis, variables were handled as follows. The variable "employment" was aggregated into three categories: student, worker, and unemployed. The divorced/widowed responses at "partner status" variable was classified as single. The age was subsequently categorized into pre-defined intervals, generating the new variable "age class". For the multivariable analysis, the independent variable "I know of the existence of the travel medicine clinic" was generated starting from the question "Clinic consultation frequency", if "Never/I never heard of it" the answer of the new variable is "No", if "Whenever before making a trip/Only for travel outside of Europe" the response of the new variable is "Yes". Both absolute and relative frequencies were calculated for all qualitative variables; Pearson's chi-square test (χ^2) was used to analyse categorical variables. A multivariable logistic regression was performed, considering low knowledge as a dependent variable (median of error >3).

The statistical significance level for the analyses was 0.05. In model 1 we did not perform any adjustment, model 2 was adjusted for age and gender. Results are expressed as crude odds ratio (OR) (model 1) and adjusted OR (aOR) (model 2) with 95% confidence intervals (95% CI). The data were analysed using the STATA statistical software version 14 (StataCorp. 2015. College Station, TX, US).

RESULTS

Descriptive characteristics of the sample (n = 1119)are presented in Table 1. Respondents had a mean age of 37.3 year (with 12.4 SD) and 68.4% were women. On overage, they were mainly Italian (98.8%), highly educated (59.1%) and employed (41.6). In most of the cases (55%) respondents had never heard about or never attended travel medicine clinic. Table 2 shows the frequency of replies on knowledge and attitude regarding ZIKV in the total sample stratified by level of knowledge. In total, 20.2% (n = 226) and 71.4% (n = 798) of the sample knew the etiological agent and transmission route of ZIKV infection, respectively. Among those with an overall good level of knowledge, only 27.3% correctly identified a virus as etiological agent, whist the majority (67.2%) thought that the cause of the infection was a mosquito. As regards the need of prevention measures to be taken before travelling abroad, 59.3% of the total sample was aware of them, and 83.1% among those very knowledgeable about ZIKV. Approximately 43% of the sample declared to not knowing the measures to prevent the risk of transmission of infection after returning from endemic areas, both in case of ex-

Table 1

Descriptive characteristics of the study population

•				
Variables		Ν	%	
Sex	Female	765	68.4	
	Male	354	31.6	
Age (mean ± SD)	37.3 ± 12.4			
Age class	18-25	167	14.9	
	26-35	463	41.4	
	36-45	215	19.2	
	46-55	154	13.8	
	56-65	94	8.4	
	>65	26	2.3	
Nationality	Italian	1106	98.8	
	Other	13	1.2	
Region	North Italy	378	33.8	
	Central Italy	299	26.7	
	South Italy and Islands	442	39.5	
Education	Lower than university degree	661	59.1	
	University degree or higher	458	40.9	
Employment	Student	240	21.4	
	Employee			
	Freelancer	251	22.4	
	Unemployed	115	10.3	
	Retired	48	4.3	
Partner status	Engaged	620	55.4	
	Single	461	41.2	
	Divorced/widowed	38	3.4	
Travel clinic consultation frequency	Whenever before travelling abroad	95	8.5	
	Only for travel outside of Europe	411	36.7	
	Never attended/I never heard of it	613	54.8	
60 · · · · · ·				

SD: standard deviation.

periencing ZIKV symptoms or not (42.3% and 42.8%, respectively). More than 80% of these showed low level of knowledge about ZIKV (83.8% and 80.4%, respectively). Specifying a multivariate regression model (*Table 3*), the analysis found that the lower level of knowledge was associated with increasing age (aOR = 1.03; 95% CI 1.02-1.04), living in central Italy (aOR = 1.38; 95% CI 1.01-1.90) or in South Italy and Islands (aOR = 1.52; 95% CI 1.14-2.02), being poorly educated (aOR = 1.54; 95% CI 1.20-1.98), having never heard of travel medicine clinic (aOR = 3.66; 95% CI 2.15-6.23), or having never attended a travel clinic (aOR = 4.03; 95% CI 2.36-6.89).

DISCUSSION

The presented nation-wide cross-sectional study yielded important results on the level of knowledge and attitudes towards the travel-related risk due to Table 2

Frequency of replies on knowledge and attitude regarding Zika virus provided by respondents, total and stratified by knowledge. The correct answer is highlighted in grey

Variables		Total	Good knowledge	Low knowledge	X²
		N (%)	N (%)	N (%)	<i>p</i> -value
What is the cause of Zika infection?	A virus	226 (20.2)	179 (27.3)	47 (10.1)	<0.001
	Drinking contaminated water	19 (1.7)	8 (1.2)	4 (0.9)	
	Dirty environments	12 (1.1)	11 (1.7)	8 (1.7)	
	Mosquito	621 (55.5)	440 (67.2)	181 (39.0)	
	l do not know	241 (21.5)	17 (2.6)	224 (48.3)	
Which is the transmission route of the Zika infection?	Through contact with saliva	24 (2.1)	16 (2.4)	8 (1.7)	<0.001
	By means of air particles (examples: coughing or sneezing)	33 (2.9)	17 (2.6)	16 (3.5)	
	Infected mosquito bite	798 (71.4)	609 (93.0)	189 (40.7)	
	l do not know	264 (23.6)	13 (2.0)	251 (54.1)	
What do you need to do before travelling to endemic areas (where Zika virus is highly prevalent)?	Bed nets, previously treated with repellents	31 (2.8)	20 (3.0)	11 (2.4)	<0.001
	Repellent sprays in sufficient quantities for the duration of the trip	136 (12.5)	68 (10.4)	68 (14.6)	
	All of the above	664 (59.3)	544 (83.1)	120 (25.9)	
	l do not know	288 (25.7)	23 (3.5)	265 (57.1)	
If Zika symptoms appear after returning from an endemic area, what should be done to prevent transmission of the infection?	Practicing protected sex (condoms) for at least 6 months following the onset of symptoms	567 (50.7)	522 (79.7)	45 (9.7)	<0.001
	It is not necessary to take any preventive measures	79 (7.0)	49 (7.5)	30 (6.5)	
	l do not know	473 (42.3)	84 (12.8)	389 (83.8)	
If after returning from an endemic area, NO symptoms of Zika appear, what should be done in order to reduce the risk of transmission of the infection?	Practicing protected sex (condoms) for at least 8 weeks after returning from the endemic area	479 (42.8)	453 (69.2)	26 (5.6)	<0.001
	It is not necessary to take any preventive measures	178 (15.9)	113 (17.2)	65 (14.0)	
	l do not know	462 (42.8)	89 (13.6)	373 (80.4)	
Which of the following preventive measures is necessary to take after returning from an endemic area, if the symptoms related to Zika have NOT appeared?	Avoid donating blood for at least 28 days after returning	743 (66.4)	598 (91.3)	145 (31.2)	<0.001
	It is not necessary to take any preventive measures	48 (4.3)	18 (2.8)	30 (6.5)	
	l do not know	328 (29.3)	39 (5.9)	289 (62.3)	
Before planning to travel abroad, do	Yes	632 (56.5)	502 (76.6)	130 (28.0)	< 0.001
you check if your destination is an endemic area and/or there are high- risk factors for Zika infection?	No	487 (43.5)	153 (23.4)	334 (72.0)	
Median of error = 3	Subject equal or below the median of error (if ≤3 errors)	655 (58.5)	-	-	
	Subject over the median of error (if >3 errors)	464 (41.5)			

 $Good knowledge: median of error \le 3 errors; low knowledge: median of error > 3 errors.$

ZIKV infection among general public. The first important finding is the low level of awareness and basic knowledge of ZIKV among the participants. If from one hand only 20.2% the respondents knew that responsible of Zika is a virus, from the other, the survey captured that more than two-third (71.4%) of the sample was aware of ZIKV transmission via the bite

of an infected mosquito. This proportion was slightly lower than that observed in a few similar studies, in which disparities may be attributable to differences in characteristics of the study population and settings. For instance, most of these researches were conducted among health care providers [28, 29] or in countries with a history of previous ZIKV transmission [30],

Table 3

Multivariable logistic regression model based on 1119 observations. Crude and adjusted odds ratio are presented

Dependent variable: Low knowledge (median of error >3)							
		OR (95% CI)	p-value	aOR (95% CI)	p-value		
Sex*	Female	1		1			
	Male	1.01 (0.77-1.30)	0.978	0.99 (0.77-1.29)	0.977		
Age** (continuous)	Per unit increase	1.03 (1.02-1.04)	< 0.001	1.03 (1.02-1.04)	<0.001		
Citizenship	Italian	1		1			
	Other	0.42 (0.11-1.53)	0.189	0.38 (0.10-1.44)	0.157		
Region	North Italy	Ref.		Ref.			
	Central Italy	1.51 (1.10-2.06)	0.018	1.38 (1.01-1.90)	0.045		
	South Italy and Islands	1.61 (1.21-2.13)	< 0.001	1.52 (1.14-2.02)	0.005		
Education	University degree or higher	Ref.		Ref.			
	Lower than university degree	1.75 (1.36-2.20)	< 0.001	1.54 (1.20-1.98)	<0.001		
Occupation	Student	1		1			
	Worker	1.70 (1.25-2.31)	0.001	1.08 (0.76-1.54)	0.675		
	Unemployed	2.09 (1.32-3.29)	0.002	1.49 (0.92-2.40)	0.104		
Partner status	Engaged	1		1			
	Single	0.77 (0.61-0.98)	0.039	1.09 (0.84-1.44)	0.496		
Travel clinic consultation	Whenever before travelling abroad	Ref.		1			
	Only when travelling outside Europe	1.35 1.35 (0.80-2.27)	0.257	1.41 (0.83-2.40)	0.198		
	Never heard of it	3.42 (2.03-5.79)	< 0.001	3.66 (2.15-6.23)	<0.001		
	Never	4.01 (2.36-6.81)	< 0.001	4.03 (2.36-6.89)	<0.001		

OR: odds ratio; 95%CI: 95% confidence interval; aOR: adjusted OR for age and sex; *adjusted only for age; **adjusted only for sex.

where the awareness about the diseases is expected to be higher. Contrarywise, the overall level of knowledge regarding the correct use of repellent and bed net was found in approximately half of the sample. In previous literature, prevalence of knowledge and use of bite-prevention measures varied greatly, according to different aspects of surveys design and conduction, including type and ages of travellers, studied disease, and local availability of travel medicine clinic [31, 32]. Interestingly, more than a quarter respondents reported inaccurate ZIKV transmission routes and prevention practices, mostly not knowing the correct answer for the selected items. In travel medicine research, knowledge of the infection cause and transmission route has been correlated to better compliance towards the use of prevention measures [5, 33]. In particular, mosquito-bite prevention is a basic strategy to protect from numerous vector-borne diseases. Therefore, general public should be informed and instructed on the correct use of bite-prevention measures (e.g., use of repellent, appropriate clothing, sleeping under bed net, etc.) when travelling abroad [5, 34].

Less than half of the interviewed knew the importance of practicing protected sex (through condom use) on the returning from an endemic area, over a period that ranging from 8 weeks to 6 months, based on the appearance of Zika-related symptoms. This can be considered a proxy of respondents' very low knowledge of the sexual transmission of ZIKV, also in case of asymptomatic infection, and related consequences of infection during pregnancy. The finding is concerning and reflects missed opportunities for prevention of ZIKV infection through correct practices and behaviours, as highlighted in previous studies [35-37]. Having a third of the sampled general public unaware of the importance of avoiding blood donation for at least 28 days after returning is a substantial public health issue. In fact, this might lead blood donors to not declare recent travels in Zika endemic areas. In this context, the US Centers for Disease Control and Prevention highlighted that blood donor screening on the basis of a questionnaire, without a laboratory test, is insufficient for identifying Zika-infected serum [38], likely due to donors' under-reporting of previous travels. As a matter of fact, ZIKV ribonucleic acid (RNA) persists in serum during weeks [39], and a systematic review and meta-analysis on the prevalence of ZIKV in blood donations indicated that RNA prevalence showed a high variability, reaching high-risk level in most of the situations [40].

The current study was also designed to investigate the respondents' overall level of knowledge on ZIKV. Self-reported surveys displayed a worrisome extremely high proportion of interviewees (41.5%) with an unsatisfactory awareness of ZIKV, risk of infection, and the important precautions to be taken to avoid transmission and consequences of infection during pregnancy. In multivariable analysis, increasing age, low education level, region of residence and the behaviour of not attending travel clinic before travelling predicted respondents' poor knowledge. These results can be easily explained as younger age is associated to more access to information on travel-related risk and illness, by virtue of great abilities to easily seek and obtain health information online [41], and, as expected, education background was found to influence knowledge about Zika, in line with previous surveys [42, 43]. The multivariate model also suggested that highly knowledgeable respondents were those living in the North of Italy. The country has a universal coverage National Health System that is organised on national, regional and local levels; the regional or local organization of Preventive Departments - which include Travel Clinic - may explain disparities on ZIKV-related knowledge across regions [44]. However, the regional gap in travel health information in Italy deserves further research.

As regards the behaviour of seeking medical care before travelling abroad, it is worth also noting that this study investigated respondents' knowledge and attitude towards travel medicine clinic consultation before travelling abroad. Self-reported surveys displayed a worrisome extremely low proportion of its utilization among general public. Pre-travel medical advice before travelling is the first important tool for the prevention of travel-associated illness and injuries [45, 46], and these results spotlight that specific interventions are needed to promote correct pre-travel behaviours and practices among general public, pointing key messages that focus on the most relevant aspects of a healthy and safe travel, as well as to achieve an optimal level of protection against travel-related risks [4, 47, 48].

Limitations and strengths

Although it was a nation-wide study, one of the main limitations includes the use of a convenience sample, as well as the administration of the survey via social network. These two elements may have led to a selection bias, in particular a non-response bias. In fact, individual who decided to participate may differ from those who did not apply. Participants may be more highly educated, healthier and more informed on the topic compared to non-responders. However, we believe that if any selection bias has occurred, this would have resulted in selecting more conscious people, which would result in an underestimation of the true association. Moreover, since the recruitment took place via internet, only people with available electronic device and internet connection could take part of the study. Nevertheless, approximately 60% of the Italian population has a personal computer and more than 70% has a stable connection [49], limiting the possible impact of a selection bias. Using self-reported data is another potential limitation and information bias may have been introduced into this study. In fact, self-reporting data may be prone to recall bias or social desirability bias. However, in order to mitigate this risk, we anonymized the questionnaire without including sensitive information. Moreover, it was administered

on-line, which is usually associated with a lower level of social desirability bias [50]. Further, we used a validated questionnaire, and even if an information bias may not be completely excluded, this is a well-known method to reduce it.

Another limitation is associated with the lack of questions investigating the travel frequency of the interviewed people in the used research survey [25], preventing from adjusting the results according to this information, which may be considered a predictor of respondents' knowledge and risk perception towards ZIKV.

Despite these limitations, this study has some important strengths. First, since the questionnaire was based on mandatory answers, there were no missing data. Second, the administration way was very unexpensive, easy to fill and allowed to reach a high number of subjects in all the Italian regions, achieving a large and representative sample size of the Italian general population. Lastly, the questionnaire was based on multiple-choice that largely facilitate the analysis, even if it may have probably limited further exploration of such a composite phenomenon.

CONCLUSION

In the next years, the number of international travellers visiting Zika-endemic areas is expected to increase. This study offers an important insight on the low levels of knowledge and attitude towards ZIKV in Italy. The specific recommendations and information to the travellers who visit ZIKV endemic areas are available on the institutional and travel's medicine websites, but they should also be made available to the general public through dedicated websites and social media, to increase risk perception and ensure appropriate protection measures to be taken to avoid the infection and its consequences.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-forprofit sectors.

Conflict of interest statement

Authors have no competing interests to declare.

Author's contribution statement

VG and DN conceived the work, performed the study, collected data and performed data curation. OES performed data analysis. SP contributed in reporting. FP helped in collecting evidence. All authors wrote the first draft of the manuscript. VG critically revised the manuscript. All Authors read and approved the final version of the manuscript.

Data availability statement

The data sets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Received on 1 November 2021. Accepted on 13 December 2021.

REFERENCES

- Signorelli C, Odone A, Gianfredi V, Bossi E, Bucci D, Oradini-Alacreu A, et al. COVID-19 mortality rate in nine high-income metropolitan regions. Acta Biomed. 2020;91(9-S):7-18.
- Baker RE, Mahmud AS, Miller IF, Rajeev M, Rasambainarivo F, Rice BL, et al. Infectious disease in an era of global change. Nat Rev Microbiol. 2021 [online first].
- 3. Ferrara P, Masuet-Aumatell C, Ramon-Torrell JM. Acceptance of yellow fever vaccine in the older traveller: a cohort study. Acta Biomed. 2021;92(4):e2021098.
- 4. Ferrara P, Masuet-Aumatell C, Ramon-Torrell JM. Pretravel health care attendance among migrant travellers visiting friends and relatives (VFR): a 10-year retrospective analysis. BMC Public Health. 2019;19(1):1397.
- Del Prete V, Mateo-Urdiales A, Bueno-Cavanillas A, Ferrara P. Malaria prevention in the older traveller: a systematic review. J Travel Med. 2019;26(7).
- Signorelli C, Odone A, Gianfredi V, Bossi E, Bucci D, Oradini-Alacreu A, et al. The spread of COVID-19 in six western metropolitan regions: a false myth on the excess of mortality in Lombardy and the defense of the city of Milan. Acta Biomed. 2020;91(2):23-30.
- Balasco N, D'Alessandro V, Ferrara P, Smaldone G, Vitagliano L. Analysis of the time evolution of COVID-19 lethality during the first epidemic wave in Italy. Acta Biomed. 2021;92(2):e2021171.
- Rawal G, Yadav S, Kumar R. Zika virus: An overview. J Family Med Prim Care. 2016;5(3):523-7.
- Marban-Castro E, Gonce A, Fumado V, Romero-Acevedo L, Bardaji A. Zika virus infection in pregnant women and their children: A review. Eur J Obstet Gynecol Reprod Biol. 2021;265:162-8.
- Gregory CJ, Oduyebo T, Brault AC, Brooks JT, Chung KW, Hills S, et al. Modes of transmission of Zika Virus. J Infect Dis. 2017;216(Suppl. 10):S875-S83.
- Chang C, Ortiz K, Ansari A, Gershwin ME. The Zika outbreak of the 21st century. J Autoimmun. 2016;68:1-13.
- Safadi MAP, Almeida FJ, de Avila Kfouri R. Zika virus outbreak in Brazil - Lessons learned and perspectives for a safe and effective vaccine. Anat Rec (Hoboken). 2021;304(6):1194-201.
- World Health Organization. WHO Director-General summarizes the outcome of the Emergency Committee regarding clusters of microcephaly and Guillain-Barré syndrome. Geneva: WHO; 2016. Available from: www. who.int/news/item/01-02-2016-who-director-generalsummarizes-the-outcome-of-the-emergency-committee-regarding-clusters-of-microcephaly-and-guillainbarr%C3%A9-syndrome.
- Rodriguez-Valero N, Borobia AM, Lago M, Sanchez-Seco MP, de Ory F, Vazquez A, et al. Zika Virus Screening among Spanish Team Members After 2016 Rio de Janeiro, Brazil, Olympic Games. Emerg Infect Dis. 2017;23(8):1426-8.
- Hamilton B, Exeter D, Beable S, Coleman L, Milne C. Zika Virus and the Rio Olympic Games. Clin J Sport Med. 2019;29(6):523-6.
- Burattini MN, Coutinho FA, Lopez LF, Ximenes R, Quam M, Wilder-Smith A, et al. Potential exposure to Zika virus for foreign tourists during the 2016 Carnival and Olympic Games in Rio de Janeiro, Brazil. Epidemiol Infect. 2016;144(9):1904-6.
- World Health Organization. Zika strategic response framework and joint operations plan, January-June 2016. Geneva: WHO; 2016.

- World Health Organization. Zika strategic response plan quartely updated July-September 2016. Geneva: WHO; 2016.
- US Centers for Disease Control and Prevention. CDC models risk of zika virus importation resulting from travel to the 2016 Olympic and Paralympic Games 2016. Atlanta: CDC; 2016. Available from: www.cdc.gov/media/ releases/2016/s0713-paralympic-games-risks.html.
- Lucey DR. Time for global action on Zika virus epidemic. BMJ. 2016;352:i781.
- Venturi G, Zammarchi L, Fortuna C, Remoli ME, Benedetti E, Fiorentini C, et al. An autochthonous case of Zika due to possible sexual transmission, Florence, Italy, 2014. Euro Surveill. 2016;21(8):30148.
- Negri A, Arnoldi I, Brilli M, Bandi C, Gabrieli P, Epis S. Evidence for the spread of the alien species Aedes koreicus in the Lombardy region, Italy. Parasit Vectors. 2021;14(1):534.
- 23. Gradoni F, Bertola M, Carlin S, et al. Geographical data on the occurrence and spreading of invasive Aedes mosquito species in Northeast Italy. Data Brief. 2021;36:107047.
- Cheema S, Maisonneuve P, Weber I, Fernandez-Luque L, Abraham A, Alrouh H, et al. Knowledge and perceptions about Zika virus in a Middle East country. BMC Infect Dis. 2017;17(1):524.
- 25. Gianfredi V, Bragazzi NL, Nucci D, Zanella F, Martinelli D, Camilloni B, et al. Design and validation of a self-administered questionnaire to assess knowledge, attitudes and behaviours about Zika virus infection among general population in Italy. A pilot study conducted among Italian residents in public health. Epidemiol Biostat Publ Health. 2017;14(4):e12662-1-e-8.
- Morera OF, Stokes SM. Coefficient alpha as a measure of Test Score Reliability: Review of 3 popular misconceptions. Am J Publ Health. 2016;106(3):458-61.
- 27. Taber KS. The use of Cronbach's Alpha when developing and reporting research instruments in science education. Res Sci Educ. 2018;48(6):1273-96.
- Lim KY, Tham HW. Knowledge, awareness, and perception of Community Pharmacists to Zika virus infection in Klang Valley, Malaysia. Health Serv Insights. 2020;13:1178632920921425.
- 29. Rabbani SA, Mustafa F, Shouqair T, Mohamad I, Tahsin N. Zika virus disease knowledge among the future healthcare providers of the United Arab Emirates. J Adv Pharm Technol Res. 2018;9(1):20-5.
- Arief M, Hassali MA, Saleem F, Khan MU, Ahmad A, Bhagavathulha AS, et al. A cross-sectional survey on the knowledge and attitudes towards Zika virus and its prevention among residents of Selangor, Malaysia. J Pharm Pract Commun Med. 2017;3(2):81-9.
- 31. Davlantes EA, Tan KR, Arguin PM. Malaria risk in travellers: a holistic approach is needed. J Travel Med. 2018;25(1).
- 32. Rodrigues KMP, Costa A, Santoro-Lopes G. Adherence to malaria prophylaxis among travelers from a middle-income country. Rev Soc Bras Med Trop. 2019;52:e20190014.
- Ferrara P, Masuet-Aumatell C, Aguero F, Ramon-Torrell JM. Stand-by emergency treatment (SBET) of malaria in Spanish travellers: a cohort study. Malar J. 2018;17(1):134.
- 34. Alpern JD, Dunlop SJ, Dolan BJ, Stauffer WM, Boulware DR. Personal protection measures against mosquitoes, ticks, and other arthropods. Med Clin North Am.

2016;100(2):303-16.

- 35. Borges ALV, Moreau C, Burke A, Dos Santos OA, Chofakian CB. Women's reproductive health knowledge, attitudes and practices in relation to the Zika virus outbreak in northeast Brazil. PLoS One. 2018;13(1):e0190024.
- Nelson EJ, Luetke MC, Kianersi S, Willis E, Rosenberg M. Knowledge and perceptions of Zika virus transmission in the community of Puerto Plata, Dominican Republic. BMC Infect Dis. 2019;19(1):339.
- Santangelo OE, Provenzano S, Grigis D, Terranova A, D'Anna G, Armetta F, et al. Why nursing students have sex without condom? A study in the university of Palermo. Clin Ter. 2020;171(2):e130-e6.
- US Centers for Disease Control and Prevention. Zika and blood transfusion. Atlanta: CDC; 2018. Available from: www.cdc.gov/zika/transmission/blood-transfusion. html.
- Paz-Bailey G, Rosenberg ES, Doyle K, Munoz-Jordan J, Santiago GA, Klein L, et al. Persistence of Zika virus in body fluids. Final Report. The New Engl J Med. 2018;379(13):1234-43.
- 40. Liu R, Wang X, Ma Y, Wu J, Mao C, Yuan L, et al. Prevalence of Zika virus in blood donations: a systematic review and meta-analysis. BMC Infect Dis. 2019;19(1):590.
- Finney Rutten LJ, Blake KD, Greenberg-Worisek AJ, Allen SV, Moser RP, Hesse BW. Online health information seeking among US adults: Measuring progress toward a Healthy People 2020 Objective. Public Health Rep. 2019;134(6):617-25.
- 42. Heitzinger K, Thoroughman DA, Porter KA. Knowledge, attitudes, and practices of women of childbearing age

- 43. Guo F, Norton AR, Fuchs EL, Hirth JM, Garcia-Blanco MA, Berenson AB. Provider-patient communication about Zika during prenatal visits. Prev Med Rep. 2017;7:26-9.
- 44. Garattini L, Badinella Martini M, Zanetti M. The Italian NHS at regional level: same in theory, different in practice. Eur J Health Econ. 2021.
- Gianfredi V, Moretti M, Gigli M, Fusco-Moffa I. Identikit of the Umbrian traveller: analysis of clinical activity in a travel medicine unit, Italy. Ann Ist Super Sanità. 2019;55(1):63-7.
- Gianfredi V, Albano L, Basnyat B, Ferrara P. Does age have an impact on acute mountain sickness? A systematic review. J Travel Med. 2020;27(6).
- 47. Ferrara P, Masuet-Aumatell C, Aguero F, Ramon-Torrell JM. The use of stand-by emergency treatment (SBET) for malaria in travellers: A systematic review and meta-analysis of observational studies. J Infect. 2018;77(6):455-62.
- Provenzano S, Santangelo OE, Armetta F, Gianfredi V, Firenze A. iViaggio: the app for safe traveling. Minerva Med. 2019;110(5):483-5.
- Istituto Nazionale di Statistica (Italian National Institute of Statistics). Internet - sex, age, educational level. Rome: ISTAT; 2020. Available from: http://dati.istat.it/?lang=en.
- Kesse-Guyot E, Assmann K, Andreeva V, Castetbon K, Mejean C, Touvier M, et al. Lessons learned from methodological validation research in e-epidemiology. JMIR Pub Health Surveill. 2016;2(2):e160.