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Original Article

Spatial and Temporal Analysis of Meningitis Cumulative Incidence in Iran, 2011-2022

Maryam Ghalandari [1], ***Ali Dehghani*** [2], ***Seyed Mohsen Zahraei*** [3], ***Mohammad Hassan Lotfi*** [2], ****Farzan Madadizadeh*** [1,4]

1. *Department of Biostatistics and Epidemiology, School of Public Health, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*
2. *Department of Biostatistics and Epidemiology, School of Public Health, Social Determinants of Health Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran*
3. *Center for Communicable Diseases Control, Ministry of Health and Medical Education, Tehran, Iran*
4. *Medical Informatics Research Center, Institute for Futures Studies in Health, Kerman University of Medical Sciences, Kerman, Iran*

***Corresponding Author:** Email: madadizadehfarzan@gmail.com

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Abstract

Background: Meningitis is a public health challenge and one of the plans of the WHO is to defeat meningitis by 2030. This study was conducted to determine the trend of cumulative incidence and to draw a geographic map of meningitis in Iran.

Methods: Data on the cases of Fever and Neurological Symptoms Syndrome was obtained from the national surveillance system from 2011 to 2022. The cumulative incidence of meningitis was calculated for each year. Joinpoint version 5.4.0 and ArcGIS Desktop (ArcMap) 10.8.2 were used to investigate the trend of the disease incidence and identify the high-risk areas, respectively.

Results: Overall, 18,500 (24.35%) of the total cases were reported as confirmed and probable cases of meningitis. The cumulative incidence of bacterial meningitis decreased significantly in all age groups (P<0.05). The incidence of viral meningitis decreased in all ages and the population under 5 years (P<0.05). The incidence of Hib meningitis decreased in the population under 5 yr from 2015-2019 (P<0.05). The incidence of meningitis from all forms decreased in all ages and populations under 5 yr but increased in the population over 5 yr from 2011 to 2019, though these changes were not statistically significant.

Conclusion: The incidence of bacterial and viral meningitis has decreased in Iran similar to most parts of the world. The decrease in the incidence of Hib meningitis after the implementation of the vaccination in children under 5 yr emphasizes the importance of continuing Hib vaccination and integrating pneumococcal and meningococcal vaccinations into the national vaccination program.

Keywords: Incidence; Meningitis; Bacterial; Haemophilus; Viral; Spatio-temporal analysis; Iran

Introduction

Meningitis is the most common form of infectious disease of the nervous system (1) and despite the progress in the production of strong antimicrobial drugs, the invention of vaccines, and improvements in the process of disease care, it is one of the main challenges of public health in

worldwide (2, 3). Meningitis is caused by viral, bacterial, and fungal infectious agents (4) as well as non-infectious causes like drugs and autoimmune diseases (5). Acute viral meningitis is the main cause of non-infectious meningitis (4) and more than 80% of bacterial meningitis cases are caused by Streptococcus pneumoniae (pneumococcus), Haemophilus Influenzae type b (Hib) meningitis, and Neisseria meningitidis (meningococcus) (6).

The incidence rate of the disease varies from one region to another, from approximately 0.9 per 100,000 person-years in high-income countries to 80 per 100,000 person-years in low-income countries (7). The annual incidence of meningitis in Iran varies from 2.27 per 100,000 population in 2008 to 2.72 per 100,000 population in 2013 (8). More than 2.5 million new cases of bacterial meningitis and more than 236,000 deaths were reported worldwide in 2019 (9). In low-income countries, bacterial meningitis has a mortality rate of up to 54%, and up to 24% of those who survive suffer from neurological complications (7).

Risk factors such as malnutrition, family overcrowding, HIV infection, lack of immunization, indoor air pollution, and sickle cell disease make people susceptible to meningitis (10). The clinical diagnosis of meningitis is based on the presence of classic symptoms like fever, headache, and neck stiffness, or sudden onset of hemorrhagic rash with fever and its laboratory diagnosis including the analysis of cerebrospinal fluid (CSF), blood, and petechial lesions smears (11). Diagnosis can be challenging due to non-specific symptoms, particularly in infants, and the limitation in the availability of timely CSF analysis (10).

Viral meningitis can recover without treatment (12), but bacterial meningitis poses a significant global burden, especially in low-income countries. The main treatment of the disease is antibiotics and in some cases surgery. However, in the absence of timely diagnosis and correct treatment, it may lead to irreversible damage such as long-term neurological consequences, hearing loss, learning disability, motor impairment, epilepsy, and death (5). Recognizing the importance of this public health challenge, WHO has launched a roadmap to defeat meningitis by 2030, aiming to eliminate epidemics, reduce cases and deaths, and improve the quality of life (13).

In Iran, the population-based national surveillance system provides valuable data on disease demographics, trends, potential epidemics, and geographic distribution, which is crucial for addressing this public health challenge (8).

Epidemiological investigation and determination of disease trends in different regions of the world is essential. Comparing the trend and geographical distribution of meningitis helps us to identify areas with a high concentration of the disease and provides an opportunity to allocate the facilities, control the disease, and prevent epidemics on a large scale. This study was conducted to determine the trend of cumulative incidence and draw a geographic map of meningitis in Iran.

Methods

This descriptive study was conducted in Iran, a country located in West Asia with an area of 1,648,195 km^2. This country includes 31 provinces and its population was estimated at 79,926,270 in 2016 census.

Data source

The study collected nationwide data on fever and neurological symptoms syndrome cases, including demographic details, diagnostic information, vaccination history, clinical characteristics, and outcomes. Data was extracted from the national surveillance system in an Excel file from Mar 21, 2011, to Mar 20, 2022.

Case definition

The diagnosis of meningitis was based on national guidelines that classified patients into suspected, probable, and confirmed cases. A suspected case was any person with a fever above 38.5 °C and at least one meningeal symptom, such as neck stiffness, decreased consciousness, or other meningeal symptoms. A suspected case was considered probable if their CSF test showed abnormalities like turbidity, elevated white blood

cells, increased protein, decreased glucose, and the presence of specific bacteria in gram staining. A suspected and probable case was classified as confirmed if they had positive cultures identifying the causative bacteria in the CSF or blood, or if pathogenic antigens were detected through the Latex Agglutination Test (8).

Statistical analysis

The cumulative incidence of meningitis disease (confirmed and probable cases), bacterial and viral meningitis, Hib meningitis, and Syndrome were calculated separately for each year using the Country population as the denominator in 2012, and 2017 Censuses, and the population forecast for the year 2021. The linear interpolation method was used to obtain the population for the intervening years. Cumulative incidence of disease was reported per 100,000 population. Bacterial meningitis included Streptococcus pneumoniae, (Hib) meningitis and Neisseria meningitidis.

Joinpoint regression analysis was used to identify trend significant changes in the incidence of disease. The Average Annual Percent Changes (AAPCs) and the Annual Percent Changes (APCs) were calculated with corresponding 95% confidence intervals (95%CI)(14). The best-fit model was chosen based on the weighted Bayesian information criterion.

AAPCs were calculated for five predetermined fixed intervals: (a) the entire study period (2011–2022), (b) before the implementation of the Hib vaccination program (2011-2014), (c) after the implementation of the vaccination program and before the COVID-19 pandemic (2015-2019), (d) period after the COVID-19 pandemic (2020–2022), (e) during the period without considering the COVID-19 pandemic years (2011-2019).

In Iran, the implementation of the Hib vaccination program was on Nov 18, 2014, and the post-COVID-19 period was after the announcement of the pandemic on Mar 4, 2020.

Qualitative data was reported based on frequency and percentage. Cumulative incidence was calculated using Microsoft Excel 2016. ArcGIS Desktop (ArcMap) 10.8.2 was used to draw a geographical map of the cumulative incidence of meningitis for each province in Iran.

Joinpoint software version 5.4.0 was used to determine the trend of disease incidence. Time trends were considered statistically significant when APCs or AAPCs had a *P*-value<0.05.

The Ethics Committee of Shahid Sadoughi University of Medical Sciences reviewed and approved the study protocol. (Ethic code: IR.SSU.SPH.REC.1402.118.).

Results

Overall, 75,950 cases of fever and neurological symptoms syndrome had been reported from 2011 to 2022. 18,500 (24.3%) of the total cases were reported as confirmed and probable cases (meningitis disease). Of the total meningitis cases, the age of 8714 (47.3%) patients was less than 5 years. The gender of 11553 (62.7%) patients was male. 14443 (78.4%) patients were residents of the city. 2779 (15.3%) patients were employed. The kind of meningitis was other things in 1687 (70.8%) of confirmed cases and the outcome of death was reported in 581 (3.1%) meningitis patients (Table 1).

Information related to clinical symptoms was collected since 2016 in Iran. Overall, 36,773 cases of fever and neurological symptoms syndrome and 9,276 cases of meningitis were examined in terms of symptoms of fever, headache, vomiting, decreased consciousness, neck stiffness, seizures, Kernig, bulging fontanelle, and brudzinski. Fever was the most common sign in patients. It was reported in 88.0% of all cases and 87.4% of meningitis cases. Brudzinski was observed in 1.1% of all cases and 3.2% of meningitis cases (Fig. 1). The highest frequency of cases of syndrome and meningitis were reported in the summer, spring, autumn, and winter seasons, respectively (Fig. 2).

Table 1: The epidemiological and clinical characteristics of patients

Variables	Levels	n (%)
Classification of Fever and Neurological Symptoms Syndrome	Suspected	57450(75.6)
	Probable	16118(21.2)
	Confirmed	2382(3.1)
Age group (probable and confirmed Cases)	Under 5 years	8714(47.3)
	5-14 years	2626(14.3)
	15-44 years	4027(21.9)
	45-64 years	1846(10.0)
	>65	1196(6.5)
Sex (probable and confirmed Cases)	Female	6873(37.3)
	Male	11553(62.7)
Occupation (probable and confirmed Cases)	Children &Neonate	9893(54.6)
	Employed	2779(15.3)
	Housewife	2219(12.2)
	Student	2025(11.2)
	Unemployed	501(2.8)
	Retired	475(2.6)
	Other (a prisoner and soldier)	231(1.3)
Residency Area (probable and confirmed Cases)	Urban	14443(78.4)
	Rural, nomads, and mobile	3984(21.6)
Kind of Meningitis (confirmed cases)	S. pneumonia	385(16.2)
	N. meningitis	194(8.1)
	H. influenza	116(4.9)
	Other things	1687(70.8)
Outcome of the disease (Suspected & probable and confirmed cases)	Improved	54370(71.6)
	Death	1399(1.8)
	Unknown	20181(26.6)
Outcome of the disease (probable and confirmed cases)	Improved	13660(73.8)
	Death	581(3.1)
	Unknown	4259(23.0)

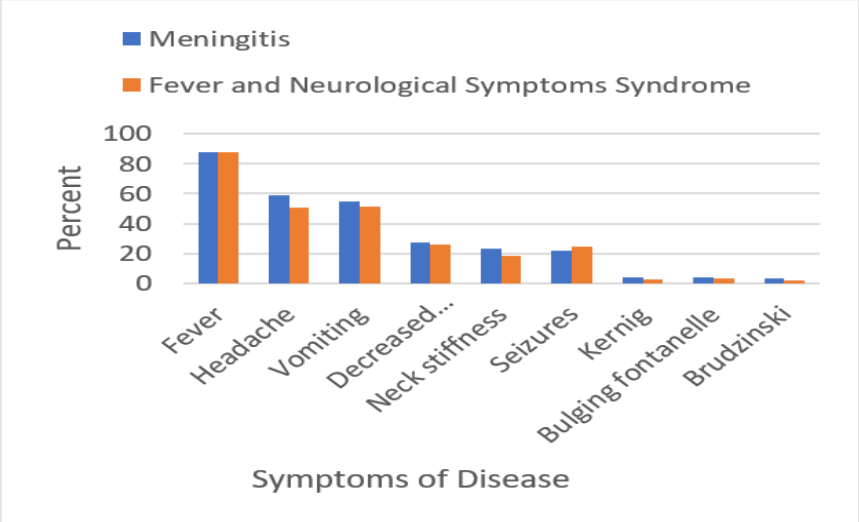

Fig. 1: Clinical symptoms of meningitis and cases of fever and neurological symptoms syndrome in Iran

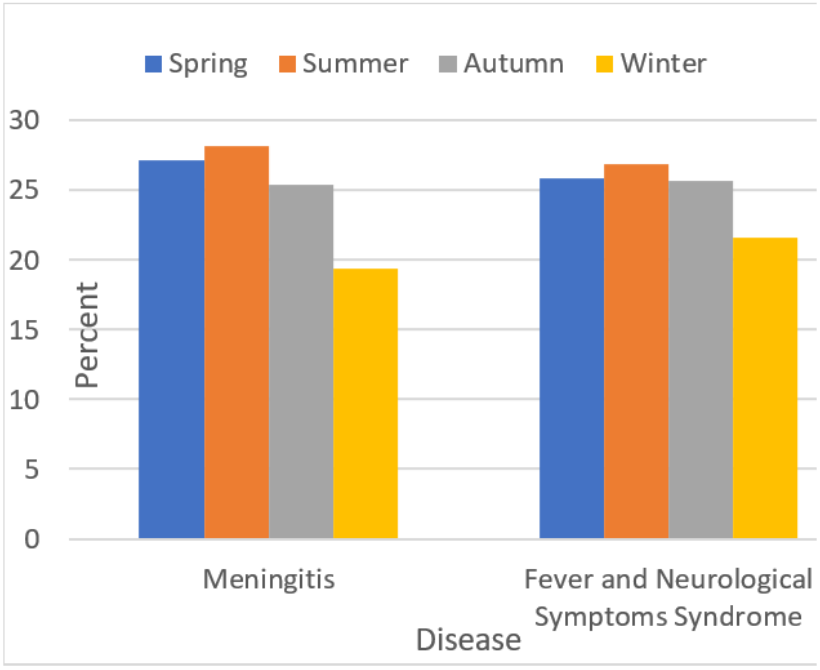

Fig. 2: Frequency of cases of meningitis and fever and neurological symptoms syndrome by season

The highest and lowest cumulative incidence of meningitis was 2.78 and 0.87 per 100,000 population in the years 2013 and 2020 in all ages.

The results incidence of the syndrome and meningitis caused by viral, bacterial, and Hib meningitis are shown in Table 2.

Table 2: Cumulative incidence of kinds of meningitis and fever and neurological symptoms syndrome

Year	Age Group	Bacterial Meningitis	Viral Meningitis	Hib Meningitis	Meningitis	All cases
		Incidence (95%CI)	Incidence (95%CI)	Incidence (95%CI)	Incidence (95%CI)	Incidence (95%CI)
2011	total	0.23(0.19-0.26)	1.14(1.10-1.20)	0.05(0.03-0.06)	2.24(2.13-2.30)	9.18(8.96-9.39)
	under 5 years	1.16(0.89-1.42)	8.50(7.80-9.19)	0.40(0.24-0.56)	12.85(12.0-13.70)	67.56(65.52-69.6)
	over 5 years	0.14(0.11-0.17)	0.47(0.40-0.50)	0.02(0.01-0.03)	1.26(1.18-1.30)	3.85(3.71-4.00)
2012	total	0.24(0.20-0.27)	1.30(1.20-1.39)	0.04(0.02-0.05)	2.40(2.29-2.51)	9.75(9.50-9.97)
	under 5 years	1.45(1.16-1.75)	9.90(9.20-10.80)	0.38(0.23-0.53)	13.80(12.90-14.7)	70.51(68.46-72.6)
	over 5 years	0.12(0.10-0.15)	0.50(0.45-0.60)	0.01(0.00-0.01)	1.33(1.24-1.42)	4.10(3.95-4.25)
2013	total	0.31(0.27-0.35)	1.58(1.50-1.70)	0.09(0.07-0.11)	2.78(2.66-2.89)	10.95(10.7-11.19)
	under 5 years	1.80(1.47-2.12)	10.60(9.80-11.00)	0.62(0.43-0.82)	14.50(13.6-15.40)	72.42(70.36-74.5)

Table 2: Continued…

	over 5 years	0.17(0.14-0.20)	0.70(0.67-0.8)	0.04(0.02-0.05)	1.66(1.56-1.75)	5.13(4.97-5.30)
2014	total	0.27(0.24-0.31)	1.54(1.50-1.60)	0.08(0.06-0.10)	2.58(2.47-2.70)	10.56(10.33-10.8)
	under 5 years	1.62(1.31-1.92)	10.35(9.60-11.0)	0.74(0.54-0.95)	14.70(13.80-15.70)	69.53(67.54-71.5)
	over 5 years	0.15(0.12-0.17)	0.69(0.60-0.80)	0.02(0.01-0.03)	1.41(1.33-1.50)	4.78(4.60-4.94)
2015	total	0.18(0.15-0.21)	1.42(1.30-1.50)	0.05(0.04-0.07)	1.98(1.88-2.08)	10.38(10.15-10.6)
	under 5 years	1.00(0.76-1.23)	9.00(8.30-9.71)	0.38(0.23-0.52)	10.56(9.80-11.30)	67.23(65.3-69.16)
	over 5 years	0.10(0.08-0.13)	0.69(0.60-0.80)	0.02(0.01-0.03)	1.15(1.07-1.23)	4.89(4.70-5.05)
2016	total	0.24(0.21-0.28)	1.24(1.20-1.30)	0.06(0.04-0.08)	2.29(2.18-2.39)	9.09(8.88-9.30)
	under 5 years	1.35(1.08-1.62)	8.68(8.0-9.40)	0.42(0.27-0.57)	12.90(12.10-13.80)	58.33(56.55-60.1)
	over 5 years	0.14(0.11-0.16)	0.52(0.50-0.60)	0.03(0.01-0.04)	1.25(1.17-1.33)	4.29(4.14-4.45)
2017	total	0.23(0.20-0.27)	1.28(1.20-1.40)	0.04(0.03-0.06)	1.98(1.89-2.08)	8.02(7.83-8.22)
	under 5 years	1.05(0.81-1.28)	9.20(8.50-9.91)	0.30(0.18-0.43)	10.55(9.80-11.30)	52.36(50.7-54.02)
	over 5 years	0.15(0.13-0.18)	0.50(0.45-0.60)	0.02(0.01-0.03)	1.14(1.07-1.22)	3.66(3.53-3.80)
2018	total	0.26(0.23-0.30)	1.50(1.40-1.60)	0.07(0.06-0.09)	2.50 (2.41-2.63)	9.93(9.71-10.14)
	under 5 years	1.19(0.94-1.45)	9.80(9.10-10.60)	0.38(0.23-0.52)	12.3(11.50-13.10)	55.95(54.22-57.7)
	over 5 years	0.17(0.14-0.20)	0.70(0.67-0.80)	0.05(0.03-0.06)	1.58(1.49-1.67)	5.50(5.33-5.66)
2019	total	0.13(0.11-0.16)	0.94(0.90-1.00)	0.02(0.01-0.03)	2.36(2.25-2.46)	8.82(8.60-9.02)
	under 5 years	0.57(0.40-0.75)	6.20 (5.65-6.80)	0.13(0.04-0.21)	11.10(10.30-11.90)	49.99(48.3-51.65)
	over 5 years	0.09(0.07-0.11)	0.45(0.40-0.50)	0.01(0.01-0.02)	1.55(1.46-1.64)	5.02(4.86-5.18)
2020	total	0.02(0.01-0.03)	0.27(0.20-0.30)	0.00(0.00-0.01)	0.87(0.81-0.94)	3.30(3.18-3.40)
	under 5 years	0.19(0.09-0.30)	2.29(1.90-2.70)	0.04(0.01-0.10)	6.67(6.05-7.29)	25.95(24.7-27.20)
	over 5 years	0.01(0.00-0.02)	0.10(0.08-0.10)	0.00(0.00-0.00)	0.37(0.32-0.41)	1.32(1.24-1.40)
2021	total	0.02(0.01-0.04)	0.30(0.27-0.30)	0.00(0.00-0.00)	1.30(1.23-1.38)	5.74(5.58-5.90)
	under 5 years	0.11(0.03-0.19)	2.61(2.20-3.00)	0.00(0.00-0.00)	8.82(8.10-9.55)	39.12(37.6-40.65)
	over 5 years	0.02(0.01-0.03)	0.11(0.10-0.10)	0.00(0.00-0.00)	0.68(0.63-0.74)	2.99(2.86-3.11)

Joinpoint regression analysis showed the cumulative incidence of bacterial meningitis decreased significantly in all age groups and the incidence of viral meningitis decreased significantly in all ages, and in the population under 5 years in the years 2015-2019 and 2011-2019 (P<0.05).

The cumulative incidence of Hib meningitis decreased significantly in the age group under 5 years in the years 2015-2019 (AAPC:-24.2-%95CI:-43.5--11), (P<0.05). So that, a 24% reduction in the average incidence was seen annually in the population under 5 years in this period. This decreasing trend was observed in all age groups in 2011-2019, although it was not statistically significant (P>0.05).

The cumulative incidence of viral, bacterial, and Hib meningitis decreased significantly in all ages and both age groups in the years 2020-2022 (P<0.05).

The incidence of meningitis from all forms decreased in all ages and age groups under 5 years but increased in age groups over 5 years in the years 2011-2019 and 2015-2019. However, these changes were not statistically significant. A decreasing trend of incidence was observed in all ages, and in both age groups in the years 2020-2022 that was not statistically significant(P>0.05).

The cumulative incidence of the syndrome has significantly decreased in all periods, in the population under 5 yr old, (AAPC:-6.4- % 95CI:-9.8--3.3) (P<0.05). Models without any breakpoints were selected as the best models for the syndrome in all age groups from 2011 to 2022. Since the model did not show any break-point, AAPCs were the same as APCs. The results are shown in Table 3 and Fig. 3(a-e).

Table 3: Analysis of the cumulative incidence kinds of Meningitis in Iran, by age groups during the years 2011-2022

Agent/ Age Group	Year	APC	2011-22	2011-14	2015-19	2020-22	2011-19
		APC (95% CI)	AAPC (95% CI)	AAPC (95% CI)	AAPC (95% CI)	AAPC (95% CI)	AAPC (95% CI)
Bacterial Meningitis							
All ages	2011-18	-0.06(-5.5-7.2)	-21.8 (-30.5--15.7)*	-0.06(-5.5-7.2)	-18.5(-26.1--5.0)*	-55.8(-76.5--38.1)*	-9.7(-14.6--4.4)*
	2018-22	-55.8(-76.5- -38.1)*					
under 5 years	2011-18	-3.6(-9.1-3.9)	-23.7(-32.8- -17.3)*	-3.6(-9.1 -3.9)	-20.6(-28.4--6.2)*	-55.7(-80.1--36.9)*	-12.5(-17.3--6.2)*
	2018-22	-55.7 (-80.1- -36.9)*					
over 5 yr	2011-18	2.5(-4.4-13.0)	-19.0(-32.0- -12.3)*	2.5(-4.4-13.0)	-15.8(-26.1--1.7)*	-53.3(-83.0--33.7)*	-7.1(-13.3- -0.5)*
	2018-22	-53.3(-83.0- -33.7)					
Viral Meningitis							
All ages	2011-18	1.4(-4.3-11.4)	-15.1(-24.6--10.1)*	1.4(-4.3-11.4)	-12.6(-20.9--1.7)*	-43.98(-71.8--28)*	-5.8(-10.5--0.1)*
	2018-22	-43.98(-71.8- -28)*					
under 5 yr	2011-18	-0.29(-4.2-4.99)	-13.95(-18.8--10.7)*	-0.29(-4.2-4.99)	-11.8(-17.1--3.6)*	-38.9 (-54.9--27.2)*	-6.2(-9.2 --2.8)*

Table 3: Continued…

	2018-22	-38.99(-54.9- -27)*					
over 5 yr	2011-18	2.95(-5.6-44.5)	-15.6(-32.8--1.9)*	2.95(-5.6-39.7)	-12.7(-26.2-1.95)	-46.8(-85.4--16.0)*	-5.2(-12.8-6.3)
	2018-22	-46.8(-85.4- -16.0)*					
Hib Meningitis							
All ages	2011-18	1.75(-8.5-33.7)	-29.9(-62.1--7.3)*	1.75(-8.4-32.1)	-25.4 (-44.9-0.3)	-70.7(-99.1--24.4)*	-12.9(-25.8-3.3)
	2018-22	-70.7(-99.1--24.4)*					
under 5 yr	2011-14	24.2(-9.2-125.9)	-12.1 (-45.5--3.2)*	24.2(-9.2-72.6)	-24.2(-43.5--11)*	-24.2 (-91.2--16.6)*	-8.8(-21.9-2.2)
	2014-22	-24.2(-91.2--16.6)*					
over 5 yr	2011-18	11.3(-1.6-62.6)	-22.55(-52.8-4.2)	11.3(-1.65-57.7)	-17.7(-37.5-13.7)	-66.8(-98.0--15.7)*	-4.3(-17.4-16.9)
	2018-22	-66.7(-98.02--15.7)*					
Meningitis (confirmed and probable cases)							
All ages	2011-19	-1.5(-14.8-39.8)	-7.95(-15.5-0.6)	-1.5(-13.7-24.4)	-1.47(-13.4- 4.2)	-29.88(-54.8-0.6)	-1.47(-7.87-4.9)
	2019-22	-29.88(-54.9-0.6)					
under 5 yr	2011-22	-4.7(-9.8-0.24)	-4.7(-9.8-0.24)	-4.7(-9.8 -0.24)	-4.7(-9.8 -0.24)	-4.7(-9.8-0.24)	-4.7(-9.8 -0.24)
over 5 yr	2011-19	0.18(-14.5-60.0)	-8.7(-18.7-2.9)	0.19(-13.9-34.7)	0.19(-14.8-7. 6)	-37.05(-65.4-1.6)	0.19(-7.8-8.5)
	2019-22	-37.05(-65.4-1.6)					
Fever and Neurological Symptoms Syndrome							
All ages	2011-22	-4.9(-9.9-0.004)	-4.9(-9.9-0.004)	-4.9(-9.9-0.004)	-4.9(-9.9-0.004)	-4.9(-9.9-0.004)	-4.9(-9.9-0.004)
under 5 yr	2011-22	-6.4(-9.8--3.33)*	-6.4(-9.8--3.33)*	-6.4(-9.8--3.33)*	-6.4(-9.8--3.33)*	-6.4(-9.8--3.33)*	-6.4(-9.8--3.33)*
over 5 yr	2011-22	-2.3(-8.5-4.1)	-2.3(-8.5-4.1)	-2.3(-8.5-4.1)	-2.3(-8.5-4.1)	-2.3(-8.5-4.1)	-2.3(-8.5-4.1)

* *P*-value<0.05

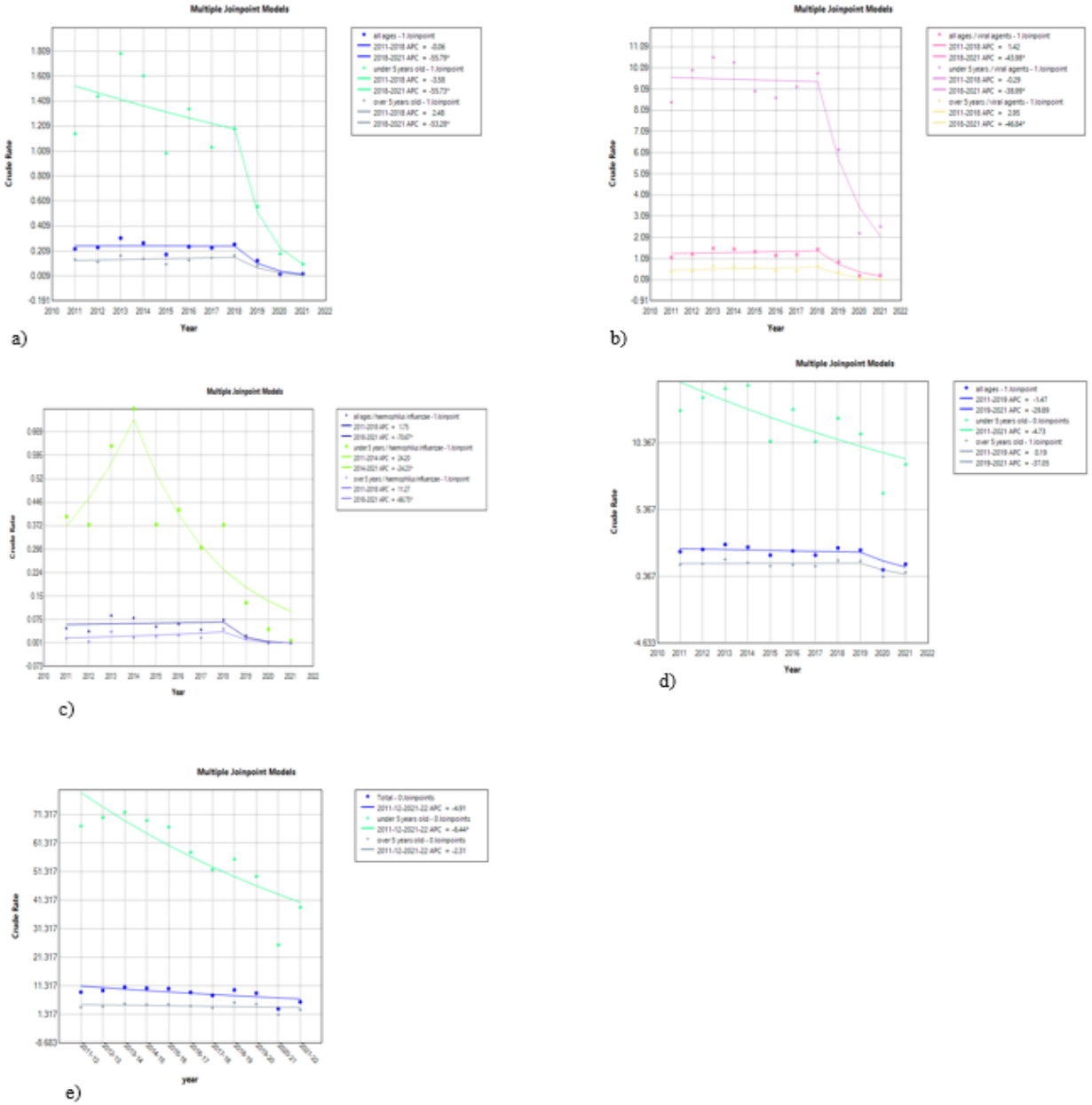

Fig. 3: The trend of the cumulative incidence kinds of Meningitis in Iran, by age groups during the years 2011-2022 a) Bacterial Meningitis b) Viral Meningitis c) Hib. Meningitis d) Meningitis e) Fever and Neurological Symptoms Syndrome

After calculating the cumulative incidence of meningitis by provinces in the investigated period, the provinces of North Khorasan, Chaharmahal and Bakhtiari, Kohgiluyeh and Boyer-Ahmad, Qazvin, Mazandaran, Qom, and Kurdistan had the highest cumulative incidence of meningitis in Iran, respectively. The highest incidence was reported in the provinces of Chaharmahal and Bakhtiari, North Khorasan, Qazvin, Kurdistan, Mazandaran, Kohgiluyeh and Boyer-Ahmad for the age group under 5 yr, and in the provinces of Qom, Zanjan, Mazandaran, Kohgiluyeh and Boyer-Ahmad, Ilam, North Khorasan, Qazvin and Khuzestan for the age group over 5 yr (Fig. 4 a-c).

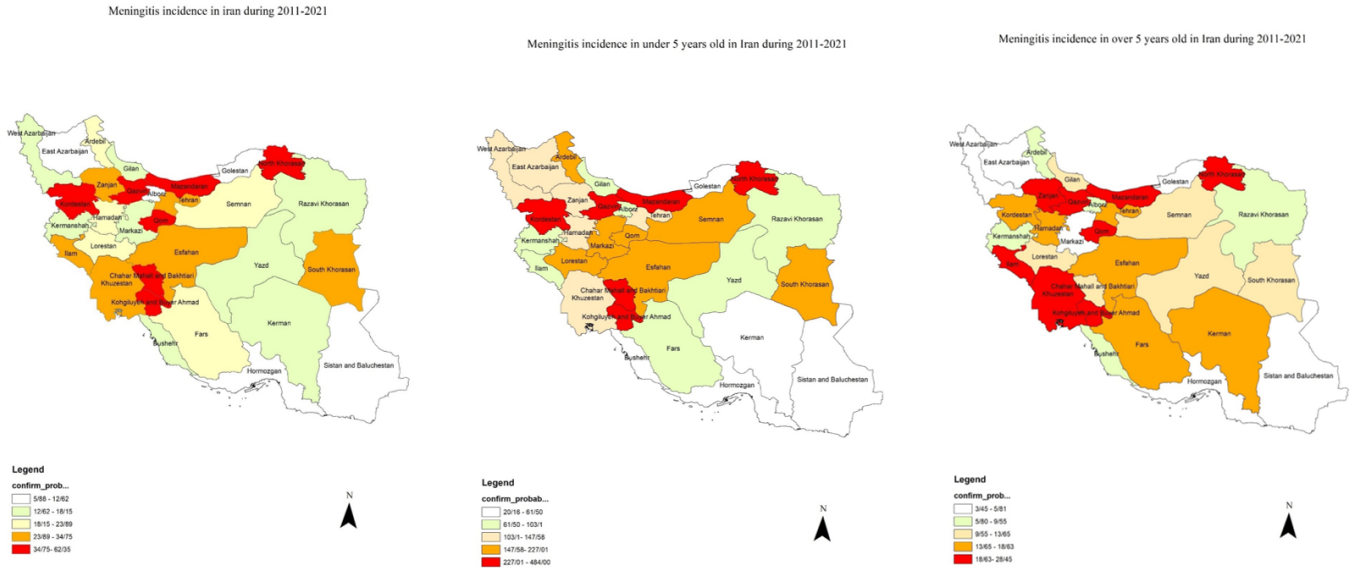

Fig. 4: Distribution of the cumulative incidence of meningitis per 100,000 in Iran, 2011-2022 a) all ages b) under 5 yr c) over 5 yr

Discussion

We analyzed 11 yr from a national meningitis surveillance database. Due to limitations in laboratory diagnosis, we reported the incidence of the disease in both confirmed and probable cases as meningitis. We also reported the cumulative incidence of cases with fever and neurological symptoms syndrome, bacterial, viral, and Hib meningitis. AAPCs were calculated for five predetermined fixed intervals.

From 2011 to 2014, the trend in the cumulative incidence of different kinds of meningitis was not statistically significant. The cumulative incidence of bacterial meningitis decreased significantly in all ages and both age groups and the incidence of viral meningitis decreased significantly in all ages and the population under 5 yr in the years 2015-2019 and 2011-2019. The cumulative incidence of Hib meningitis decreased significantly in the population under 5 yr from 2015-2019. The incidence of viral, bacterial, and Hib meningitis decreased significantly in all ages and both age groups in the years 2020-2022.

The incidence of meningitis from all forms decreased in all ages and populations under 5 yr but increased in populations over 5 yr in the years 2011-2019 and 2015-2019, though these changes were not statistically significant. The incidence of the syndrome decreased significantly in all periods for the population under 5 yr old.

The incidence of fever and neurological symptoms syndrome was reported as 9.18, 9.75, 10.95, 10.56, 10.38, 9.09, 8.02, 9.93, 8.82, 3.3, and 5.74 per 100,000 population from 2011 to 2022, respectively. The results of this study were in agreement with a study conducted in Iran during the years 2010-2015 (15), and another study conducted to investigate the impact of the vaccination program in Iran (16). The incidence of meningitis was reported as 2.24, 2.40, 2.78, 2.58, 1.98, 2.29, 1.98, 2.50, 2.36, 0.87, and 1.3 per 100,000 population from 2011 to 2022, respectively. In North West of Morocco, Kenitra Province reported the cumulative incidence of meningitis in all forms as 4.72, 4.47, 3.21, 3.98, and 6.25 from 2014 to 2018, respectively (4). The difference in the incidence of the disease is due to the difference in the geographical conditions of the countries, different age groups, and the performance of the surveillance system, especially the adequacy of the laboratory facilities to diagnose cases.

In this study, similar to other studies conducted in different parts of the world, the trend of the incidence of bacterial meningitis was decreasing (17-22). This phenomenon can be attributed to reasons such as increased monitoring of the surveillance system, early diagnosis, progress in the treatment process, improvement of living standards, health education, ease of access to health care services, and preventive measures such as widespread prescribing of meningitis vaccination or underreporting and poor monitoring related to the meningitis surveillance program.

In Iran, the incidence of meningitis had increased from 9.77 in 2009 to 10.33 in 2014 (15). In our study, incidence cases of viral and Hib meningitis were increasing in all ages until 2018. At ages less than 5 yr, this increasing trend in Hib meningitis was observed until 2014. At ages over 5 yr, this trend was observed in viral, bacterial, and Hib meningitis until 2018 and in meningitis of all forms until 2019. This increasing trend was not statistically significant in any of the examined cases. The reasons for this increasing trend were the changes in the way of reporting and direct recording of the information on fever and neurological symptoms syndrome in the Communicable Disease Control portal by universities of medical sciences across the country. This may partially justify the increase in disease reporting (15).

Results of our study also showed that the incidence of all kinds of meningitis decreased after the COVID-19 pandemic. During the pandemic, due to the high transition of the disease and the allocation of most of the health and treatment forces to control this disease, there would be underreporting in the care and control of other infectious diseases. This phenomenon also can be attributed to interventions such as increasing hand hygiene, using masks, isolation, quarantine, and restrictions on travel.

In our study, death was observed in 3.1% of meningitis cases and 1.8% of all reported cases. In Iran, the outcome of death was observed in 2% of patients (15), in another study, the outcome of death was reported at times before and after the implementation of vaccination, which was 2.7% and 2.1%, respectively (16). In Southern Vietnam, the outcome of death was reported in 1.2% of probable cases and 8.2% of confirmed cases (17).

Non-specific symptoms and various causes make it challenging to diagnose meningitis. In this study, the most common clinical symptoms were consistent with previous studies conducted in Iran (16) and North West of Morocco (4). However, the results were in contrast to another study in South Africa (2). This difference can be due to the difference in the age groups of patients and the Study population.

The study found the provinces with the highest incidence of meningitis in all ages were North Khorasan, Chaharmahal and Bakhtiari, Kohgiluyeh and Boyer-Ahmad, Qazvin, Mazandaran, Qom, and Kurdistan. In Iran, the most reported cases of meningitis were from the provinces of Qazvin, Mazandaran, and Kurdistan (23). In another study, the highest incidence was observed in the provinces of Qazvin, Qom, Kurdistan, and North Khorasan (15). The differences in incidence across provinces may be due to variations in the sensitivity and performance of the healthcare reporting systems. In addition, the number of reported cases in some provinces indicates a severe weakness of the reporting system and it is necessary to strengthen the syndromic surveillance system and increase the awareness of health professionals in identifying and reporting cases.

Limitations of the study include the high rate of cases with unknown pathogens and other things and defects in the reporting of pathogenic agents, serotype distribution, and the outcome of the disease due to the use of secondary data sources.

The strengths of this study include the use of a long-term period of data on cases of the syndrome in all parts of Iran. Moreover, our study showed AAPCs and APCs with 95% confidence intervals and reported important changes in trend using the joinpoint regression.

Conclusion

Similar to the studies conducted in other countries, the incidence of bacterial and viral meningitis decreased in Iran during the study period. The decrease in the incidence of Hib meningitis after the implementation of the vaccination program in children under 5 yr emphasizes the importance of continuing Hib vaccination and integrating pneumococcal and meningococcal vaccinations into the national vaccination program. In addition, considering the identification of high-risk areas in the country and the weakness in the reporting system of some provinces, measures such as continuous training of health professionals in early diagnosis, increasing and strengthening the capacity of laboratories to diagnose cases, and establishing effective epidemiological surveillance is necessary to maintain the decreasing trend of incidence.

Journalism Ethics considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

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Conflict of interest

The authors declare that there is no conflict of interests.

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