EPIDEMIOLOGICAL CHARACTERISTICS, ANALYSIS AND FORECAST OF VIRAL HEPATITIS A AND E IN ZIBO CITY FROM 2015 TO 2021

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ABSTRACT

Objective:*To analyze the epidemiological characteristics of viral hepatitis A and E in Zibo City from 2015-2021, thus providing a scientific basis for evaluating and developing prevention and control strategies for hepatitis A and E.*

Methods*: A descriptive epidemiological method was utilized to statistically analyze the data of patients with hepatitis A and E in Zibo City from 2015 to 2021. A seasonal auto regression integrated moving average (ARIMA) model was run to predict the future incidence of hepatitis A and E.*

Results*: From 2015 to 2021, a total of 160 cases of hepatitis A and 302 cases of hepatitis E were reported in Zibo, with annual average incidence rates of 0.248/100,000 and 0.468/100,000, respectively. Both conditions were epidemic, but not significantly cyclical and seasonal. More men developed hepatitis A and E than women, indicating a significant difference in gender statistics (P<0.05). Hepatitis A is more prevalent among young adults and middle-aged and elderly people, 48.75% of whom are aged between 45 and 60, while most cases of hepatitis E also occur in these groups, with 75% aged between 40 and 65 years. In terms of occupation, both hepatitis A and E are predominantly found among farmers, retired people and domestic and non-working people. By the seasonal ARIMA model, it was predicted that the incidence of hepatitis A and E will remain relatively stable over the next two years, with an estimated rate of less than 1 per 100,000.*

Conclusion*: Zibo reported relatively stable incidence rates of hepatitis A and E from 2015 to 2021. The seasonal ARIMA model was a good predictor of short-term incidence trends, and can be combined with actual epidemiological characteristics to formulate scientific prevention and control strategies.*

Keywords: *Viral Hepatitis, Hepatitis, Hepatitis A and E.*

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Introduction

Hepatitis A virus (HAV) is a member of the picornavirus family that belongs to the Hepadnaviridae genus, with a genome of approximately 7.5 kb in length. It is divided by its structure and function into 5'NCR, P1, P2, P3 and 3'NCR(1). Its 5'-end is linked to a viral-encoded protein, VPg, with an internal ribosomal binding site at nt152-735, where uncapped translation, ribosome binding and translation initiation will occur. The P1 region of HAV mainly encodes four structural proteins: VP1 (1D), VP3 (1C), VP2 (1B) and VP4 (1A), while the P2 and P3 regions encode non-structural proteins. 3'NCR and 3D regions form high-level structures that facilitate binding to host proteins to constitute replication complexes and initiate negative-strand RNA synthesis(2). Only one serotype is known in HAV, but it can be divided into seven genotypes, of which genotypes I, II and VII are mainly human-derived HAV strains.

HAV continues to be the most common cause of acute hepatitis infection worldwide. The infection is primarily transmitted through ingestion of contaminated food or water, or direct contact with infected people(3,4). Its clinical symptoms include fatigue, loss of appetite, hepatomegaly, abnormal liver function, jaundice in some cases, primarily triggering acute hepatitis(5). However, the global incidence of HAV shows a declining trend due to sustained economic and social development, improved health conditions and widespread HAV vaccination(6).

Hepatitis E virus (HEV) is a single-stranded, quasi-enveloped, icosahedral RNA virus. The viral genome is a single-stranded, positive-sense RNA of 7.2 kb in length with a 7-methylguanine cap at the 5' end, three open reading frames (ORF1-3) in the middle, and a polyadenine tail at the other end. ORF1 is responsible for encoding non-structural proteins and replicating RNAs, including RNA decapping enzymes and RNA-dependent RNA polymerases. ORF2 encodes the structural proteins responsible for viral capsid formation(7), which represent antigenic sites for the generation of immune responses and are therefore potential antigens for vaccine development(8). The ORF3 protein, present only in blood-borne enveloped HEV particles, is responsible for viral replication, survival and extrusion from host cells(9). HEV comprises 8 genotypes, of which HEV 1-4 are known to infect humans, while the other three genotypes are animal hosts only(10).

Hepatitis E is an acute inflammation of the gastrointestinal tract caused by infection with HEV, mainly transmitted by the faecal-oral route. Classified into Category B notifiable infectious diseases in China(11), it is clinically characterized by sudden onset, jaundice, severe infection and poor prognosis in elderly patients with underlying liver disease, susceptibility to fulminant hepatitis with serious consequences such as liver failure, and high mortality rate(12-14). It is estimated that HEV 1 and HEV 2 together are responsible for about 2010 million infections in Asia and Africa, with acute hepatitis E accounting for 3.4 million cases. Put together, HEV infection, recognized by the World Health Organisation as a major public health issue in developing countries(15), is also estimated to cause 70,000 deaths from acute liver failure(16).

Hepatitis A and E are common and transmitted by similar routes, both resulting in severe hazards. In this paper, the epidemiological characteristics of hepatitis A and E cases reported from 2015 to 2021 based on infectious disease surveillance data in Zibo, with the aim of getting the picture of their incidence characteristics and epidemiological status in the city and providing a reference basis for developing preventive and control measures.

Materials and methods

Sources of data

Hepatitis A and E cases were pooled from the Diseases Reporting Information System under the China Information System for Diseases Control and Prevention, and population information was obtained from the Zibo Bureau of Statistics.

Method

Data were collected and collated using Excel 2019 for statistical analysis by a descriptive epidemiological method. The cases were collated and analyzed by month, region, occupation, gender and age.

The seasonal ARIMA model was used to predict the future incidence of hepatitis A and E. It is classified as an ARIMA (p, d, q) x (P, D, Q) model, where p is the autoregressive order, d the differential order and q the moving average order; P is the seasonal autoregressive order, D the seasonal differential order and Q the seasonal moving average order. Currently, ARIMA is widely applied in infectious disease forecasting. ARIMA parameters were selected by SPSS expert modeling for the period 2015-2021 to observe their autocorrelation function (ACF) and partial autocorrelation function (PACF) plots of model residuals. The model was then best-fitted on the parameters given that larger stationary R2 is better, $P > 0.05$ is validated by the Jung-Box Q-test, and smaller Bayesian information criterion (BIC) is better. After non-seasonal first order differencing, the data were shown in the series plot as a smooth series with no significant increasing or decreasing trend. Forecasts were made for each month of 2022 by using the data from 2015 to 2021.

Data statistics

SPSS Statistics was the statistical analysis tool herein. X^2 test was used for comparison of rates. $P<0.05$ was considered statistically significant.

Results

Prevalence profile

From 2015 to 2021, 160 cases of hepatitis A and 302 cases of hepatitis E were reported in Zibo. The incidence of hepatitis A ranged from 0.065/100,000 to 0.378/100,000 (6-35 cases) over the six-year period, with no deaths and an average annual incidence of 0.248/100,000; the incidence of hepatitis E ranged from 0.263/100,000 to 0.595/100,000, with an average annual incidence of 0.468/100,000 and two deaths. There were no outbreaks of hepatitis A or E during the six years. Despite a low overall incidence rate, cases of hepatitis A increased between 2018 and 2019 whereas the incidence of hepatitis E generally maintained at a low level (Figure 1).

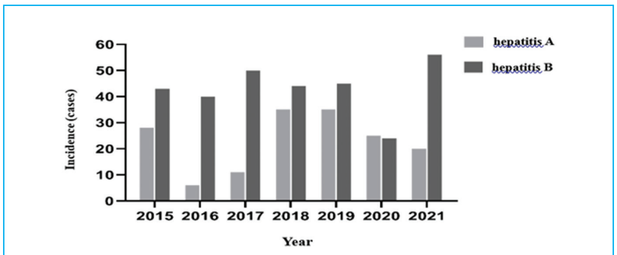

Figure 1: Cases of hepatitis A and E in Zibo from 2015 to 2021.

Prevalence features

Time-dependent distribution

From 2015 to 2021, hepatitis A was epidemic, non-cyclical and relatively stable in Zibo, with cases reported in all months of the year and no obvious seasonal clustering, whilst hepatitis E was also epidemic and non-cyclical, with cases reported in all months of the year, fluctuating in waves and relatively peaking in February-April (Figure 2).

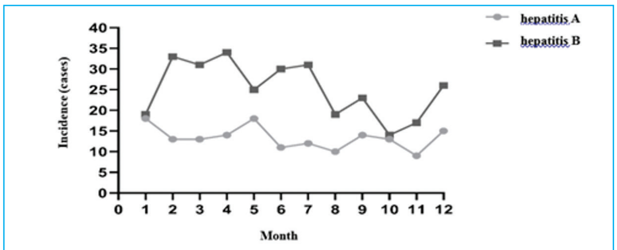

Figure 2: Time-dependent distribution of hepatitis A and E incidence in Zibo from 2015 to 2021.

Age and gender distribution

Hepatitis A was more prevalent in men than in women, with 82 male cases and 78 female cases enrolled in this study. Also, the condition was most prevalent among the population aged between 45 and 60, accounting for 48.75% of the total count (Figure 3).

Hepatitis E was more frequent in men than in women, with 212 male cases and 90 female cases enrolled in this study. It meant that the incidence was 2.35 times higher in men than in women, suggesting a significant gender distinction ($P<0.05$). Also, people aged from 40 to 65 were more susceptible to hepatitis E, accounting for 76.82% of the total count (Figure 4).

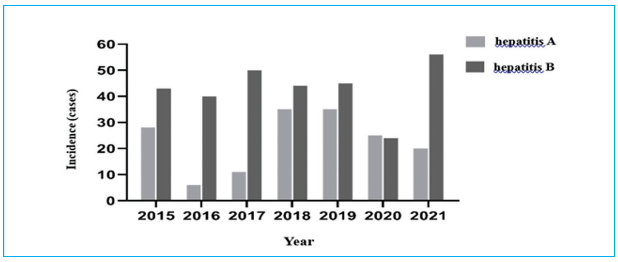

Figure 3: Incidence of hepatitis A in different age and sex groups in Zibo from 2015 to 2021.

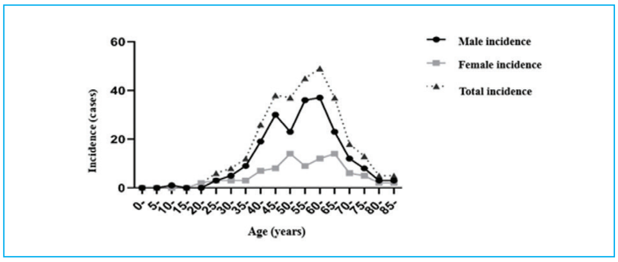

Figure 4: Incidence of hepatitis E in different age and sex groups in Zibo from 2015 to 2021.

Occupation distribution

As for occupation distribution, farmers (58.13%) were most likely to develop hepatitis A, followed by retired workers, homemakers and non-workers, accounting for 11.25% and 10.0% respectively (Figure 5); farmers (54.64%) were also most likely to develop hepatitis E, followed by retired workers, and housekeeping employees & non-working workers, accounting for 14.24% and 9.93% respectively (Figure 6).

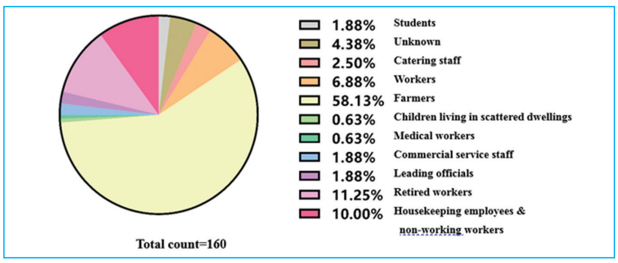

Figure 5: Incidence of hepatitis A in different occupations in Zibo from 2015 to 2021.

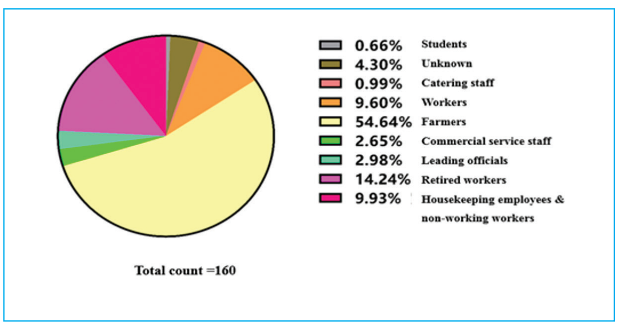

Figure 6: Incidence of hepatitis E in different occupations in Zibo from 2015 to 2021.

Regional distribution

Hepatitis A was reported in all nine districts and counties of Zibo city (Figure 7). From 2015 to 2021, Linzi District (44 cases, 27.50%), Zichuan District (30 cases, 18.75%), Zhangdian District (26 cases, 16.25%) and Boshan District (16 cases, 10.00%) notified the top four highest number of cases, all of them in the central city. Hepatitis E was also reported in all nine districts and counties of Zibo (Figure 8), and Boshan District (91 cases, 30.13%), Zhangdian District (53 cases, 17.54%), Zichuan District (44 cases, 14.56%), and Linzi District (37 cases, 12.25%) notified the top four highest number of cases, all of them in the central urban areas.

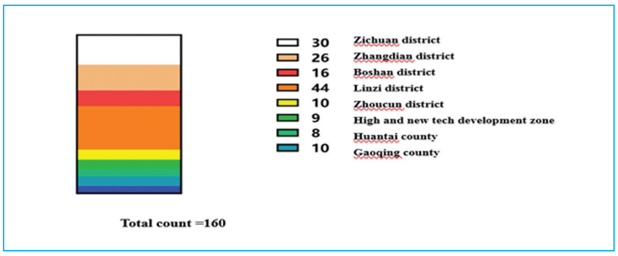

Figure 7: Incidence of hepatitis A in different regions of Zibo from 2015 to 2021.

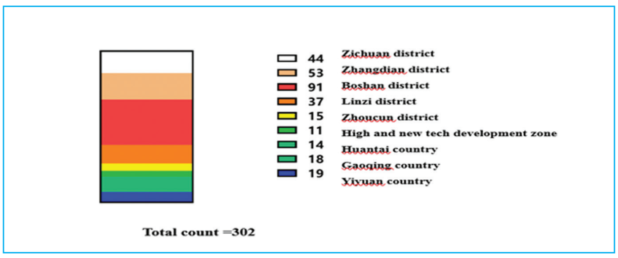

Figure 8: Incidence of hepatitis E in different regions of Zibo from 2015 to 2021.

Model-based predictions

Upon the analysis in the ARIMA model by the statistical method, it was concluded that it was feasible to predict hepatitis A cases in Zibo using the seasonal ARIMA model. The modeling based on data from 2015 to 2021 yielded a model with a stationary R2 of 0.374, an R2 of 0.260, a Jung-Box Q statistic of 11.461, a P-value of 0.245, and a standardized BIC value of 1.499 by the white noise test. As shown in Figure 9, before the vertical line was the data used to build the prediction model, indicating the monthly incidence of hepatitis E from 2015 to 2021, while after the vertical line was the predicted data. The prediction model yielded 17 new cases of hepatitis A for the year 2022 and 21 new cases of hepatitis A for the year 2023.

Likewise, the ARIMA model was used to predict the number of hepatitis E cases in Zibo. The modeling based on data from 2015 to 2021 yielded a model with a stationary R2 of 0.413, an R2 of 0.180, a Jung-Box Q statistic of 18.206, a P-value of 0.150, and a standardized BIC value of 1.859 by the white noise test. As illustrated in Figure 10, before the vertical line was the data used to build the prediction model, indicating the monthly incidence of hepatitis E from 2015 to 2021, while after the vertical line was the predicted data. The prediction model yielded 39 new cases of hepatitis E for the year 2022 and 43 new cases of hepatitis E for the year 2023.

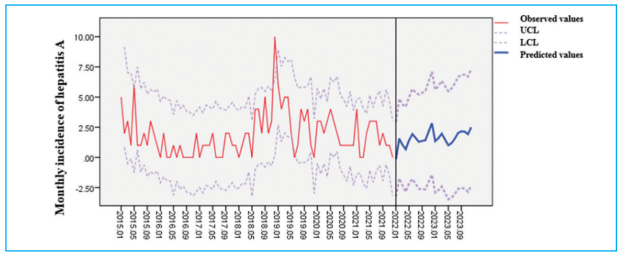

Figure 9: . Prediction results of ARIMA (1, 1, 2) (5, 0, 1) model established for hepatitis A incidence in Zibo from 2015 to 2021.

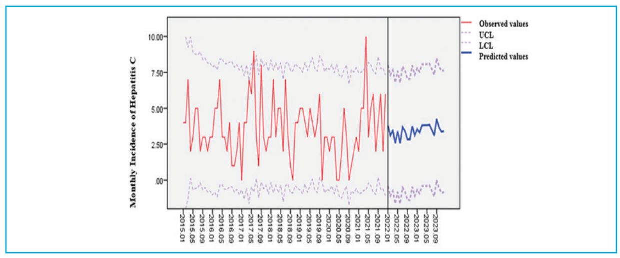

Figure 10: . Prediction results of ARIMA (1, 1, 2) (1, 0, 1) model established for hepatitis E incidence in Zibo from 2015 to 2021.

Discussion

Viral hepatitis is one of the major infectious diseases that have long plagued the health of Chinese people. It is estimated to report 1.4 million infections worldwide each year, although the global incidence of hepatitis A is on the decline with socio-economic development, improved sanitation and widespread vaccination against hepatitis A(17). In addition, no specific vaccine has been developed for hepatitis E, an important public health issue in developing countries that poses a serious threat to human life and health(18). Therefore, predicting the epidemiological trends of hepatitis A and E is of great significance for their prevention and control. In this study, the epidemiological characteristics of hepatitis A and E cases reported in Zibo from 2015 to 2021 were investigated to predict their epidemiological trends in the next two years in the seasonal

ARIMA model, thereby providing a theoretical basis for the prevention and control in Zibo city.

In Zibo City, the incidence of hepatitis A remained at a relatively low level from 2015 to 2021, despite occasional fluctuations. This was linked to the mass vaccination against hepatitis A carried out in Shandong Province in recent years, the inclusion of hepatitis A in the childhood immunization program, and the further reduction in susceptible populations(19, 20). Compared to hepatitis A, hepatitis E presented a higher level of incidence due to the absence of a specific vaccine, so precautions should be strengthened to prevent further increases.

This study was consistent with related references that from 2015 to 2021, hepatitis A was predominantly epidemic, non-cyclical and non-seasonal in Zibo(21,22), possibly due to the variation in epidemiological characteristics resulting from widespread vaccination against hepatitis A. The incidence of hepatitis E was also predominantly epidemic and non-cyclical, with cases reported in all months of the year, fluctuating in waves and relatively peaking between February and April, probably because hepatitis E is mainly transmitted via contaminated water and food, and causes more enteric infections in winter and spring. Hence, manure management and water protection should be consolidated to prevent the disease from finding its way in by the mouth and develop good living habits.

Between 2015 and 2021, both hepatitis A and E were more prevalent in males than females in Zibo City. Hepatitis E was even 2.35 times more common in men, possibly because they participated more widely in social activities and dined out more often. Among age groups, both young adults and the elderly were likely to develop the conditions. Consistent with related studies(23, 24), the 45-60 year group was the usual victims of hepatitis A, accounting for 48.75% of the total cases, while hepatitis B was most common in the 40-65 year group, accounting for 76.82%. Furthermore, both hepatitis A and E cases in this study were dominated by farmers, accounting for 58.13% and 54.64%, respectively, due to poor hygiene in rural areas, high exposure to pigs and their excreta, and lack of attention to diet and personal hygiene(25).

In Zibo, Linzi District (44 cases) experienced the highest number of hepatitis A cases from 2015 to 2021, followed by Zichuan District (30 cases), and Zhangdian District (26 cases), while Boshan District (91 cases) reported the most hepatitis E cases, followed by Zhangdian District (53 cases),

Conclusion

As predicted by the ARIMA model, the next two years will witness epidemic cases of hepatitis A and E in Zibo, so it is recommended to further reduce the incidence by promoting hepatitis A vaccination among high-risk adult groups. Meanwhile, more should be done for surveillance of the sources of infection, routes of transmission and pathogenesis of hepatitis E according to the epidemiological characteristics, and animal infections should be monitored to prevent the outbreaks of hepatitis E.

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