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Asymmetric association between meteorological factors and human infections with hemorrhagic fever with renal syndrome: A 16-year ecological trend study in Shaanxi, China

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A R T I C L E I N F O

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A B S T R A C T

Objective: Hemorrhagic fever with renal syndrome (HFRS) continues to pose a significant threat to global health. This study aimed to investigate both the long- and short-term asymmetric impacts of variations in meteorological variables on HFRS.

Methods: The reported monthly HFRS incidence data from Shaanxi between 2004 and 2019, along with corresponding meteorological data, were collected to conduct an ecological trend analysis. Subsequently, the autoregressive distributed lag (ARDL) and nonlinear ARDL (NARDL) models were used to examine the long- and short-term asymmetric effects of climate variables on HFRS incidence.

Results: Overall, a reduction in HFRS incidence was observed in Shaanxi from 2004 to 2019, with an average annual percentage change of −0.498 % (95 %*CI* -13.247 % to 12.602 %). HFRS incidence peaked in December and reached its lowest point in March each year. A 1 mm increase in aggregate precipitation (AP) was associated with a 4.3 % rise in HFRS incidence, while a 1 mm decrease contributed to a 3.7 % increase, indicating a long-term asymmetric impact (Wald long-term asymmetry test [WLT] = 9.072, $P = 0.003$). In the short term, a 1 % decrease in mean relative humidity (MRH) led to a 5.7 % decline in HFRS incidence (Wald short-term asymmetry test [WSR] = 5.978, $P = 0.015$). Additionally, changes in meteorological variables showed varied effects: ΔMWV (+) at a 1-month lag had a significant positive short-term effect on HFRS; ΔMRH(+) at a 3-month lag, ΔAP(+) at a 2-month lag, ΔAP(−) at a 1-month lag, ΔASH(+) at a 1-month lag, and ΔASH(−) at a 3-month lag all exhibited strong negative short-term impacts on HFRS incidence.

Conclusions: Weather variability plays a significant role in influencing HFRS incidence, with both long- and short-term asymmetric and/or symmetric effects. Utilizing the NARDL model through a One Health lens offers promising opportunities for enhancing HFRS control measures.

1. Introduction

Hemorrhagic fever with renal syndrome (HFRS) is a rodent-borne disease caused by hantaviruses. Human infection typically occurs through contact with contaminated droplets, inhalation of particulates, or direct contact with infected rodents and their excreta [1]. Once the virus enters the human bloodstream, it typically results in two distinct clinical presentations: Hantavirus Pulmonary Syndrome (HPS) and HFRS, which are determined by the specific hantavirus strain involved. HPS, primarily associated with Sin Nombre virus (SNV) in North

Abbreviations: HFRS, Hemorrhagic fever with renal syndrome; NARDL, Nonlinear autoregressive distributed lag; ARDL, Autoregressive distributed lag; HTNV, Hantan virus; SEOV, Seoul virus; MRH, Mean relative humidity; AP, Aggregate precipitation; MT, Mean temperature; MWV, Mean wind velocity; ASH, Aggregate sunshine hours; AAPC, Average annual percentage change; CI, Confidence interval; VIF, Variance inflation factor; ADF, Augmented Dickey–Fuller; AIC, Akaike information criterion; BIC, Bayesian information criterion; HQ, Hannan-Quinn; PACF, Partial autocorrelation function; CUSUM, Cumulative sum; CUSUM, Cumulative sum of squares; WLT, Wald long-term asymmetry; WST, Wald short-term asymmetry.

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America, manifests with symptoms such as fever, myalgia, and respiratory distress, often progressing rapidly and resulting in severe outcomes without timely medical intervention [1]. Conversely, HFRS, more common in Europe and Asia, is characterized by fever, hemorrhagic symptoms, and acute renal failure, primarily linked to the Hantaan virus (HTNV) [1,2]. In China, HTNV and Seoul virus (SEOV) are identified as the major causative agents of HFRS, with their primary natural reservoirs being *Apodemus agrarius* and *Rattus norvegicus*, respectively [3,4]. Globally, approximately 100,000 cases are reported annually, with over 90 % occurring in China, Korea, and Russia [5]. In China, HFRS is classified as a class B notifiable disease and poses a significant public health challenge [1]. From 1950 to 2014, there were 1,625,002 reported cases and 46,968 deaths in China, resulting in a death rate of 2.89 % [5]. Although the incidence of HFRS has fluctuated over recent decades, it remains one of the top nine communicable diseases in China [3]. The epidemiology of hantaviruses is largely influenced by the distribution of their reservoir hosts; however, these viruses are not uniformly present in all geographical areas inhabited by their hosts [6]. Recent studies indicate that the dual seasonal pattern of HFRS is linked to dominant hantavirus genotypes, with climate effects being more pronounced in HTNV-endemic regions compared to those dominated by SEOV [7]. This suggests that environmental factors and other potential influences should also be considered when studying the epidemiology of HFRS [6].

Research has shown that climate change can impact the epidemiology of hantavirus infections [1,6,8,9]; however, findings have been inconsistent. Most studies have employed linear models and failed to explore the long- and short-term asymmetric dynamic effects of meteorological variables on HFRS—meaning that an increase or decrease in meteorological variables may yield different effects—which is crucial for effective prevention strategies. Additionally, prior studies often overlooked the strong autocorrelations present in time series data, leading to potential overestimation. Recent research has demonstrated that the nonlinear autoregressive distributed lag (NARDL) model can address these gaps due to its several advantages [9–12]: (1) It decomposes the effect of regressors into short- and long-term components, allowing for asymmetries in various combinations of short- and long-term dynamics; (2) it accommodates time series with different orders of integration; (3) it addresses endogenous relationships between variables; and (4) it automatically considers autocorrelations in time series analysis.

Shaanxi province in central China is located between longitudes 105°29′-111°15′E and latitudes 31°42′-39°35′N and experiences a continental monsoon climate. As of 2023, its population was approximately 39.56 million. In 2005, Shaanxi had the second highest incidence rates of HFRS after Heilongjiang [3]. From 2010 to 2012, it surpassed Heilongjiang to record the highest incidence rates of HFRS [3]. However, few studies have concentrated on the influence of meteorological factors on the long- and short-term transmission dynamics of HFRS in this region. Therefore, this study aimed to conduct a 16-year ecological trend analysis to investigate the long- and short-term asymmetric dynamic associations between meteorological factors and HFRS in Shaanxi using the NARDL model.

2. Material and methods

2.1. HFRS data

The monthly HFRS incidents in Shaanxi from 2004 to 2019 were collected from the Data-center of China Public Health Science (DCPHS). Population data was sourced from the Shaanxi Statistical Yearbook. All HFRS incidents were confirmed by authorized institutions and professionals following the diagnostic criteria for HFRS (http://www.nhc.gov.cn/wjw/s9491/wsbz.shtml).

2.2. Meteorological data

Daily meteorological variables, including mean relative humidity (MRH), aggregate precipitation (AP), mean temperature (MT), mean wind velocity (MWV), and aggregate sunshine hours (ASH) were provided by the National Meteorological Science Data Center (http://data.cma.cn/), and then these variables were collated as the monthly time series format.

2.3. Statistical analysis

During the statistical description, study variables were represented as mean ± standard deviation ($\bar{x} \pm s$). The average annual percentage change (AAPC) with a 95 % confidence interval (CI) was computed to describe the epidemiological trend of HFRS [13]. Spearman's correlation was applied to test the correlation between meteorological factors and HFRS, with a correlation greater than 0.9 or a variance inflation factor (VIF) greater than 10 was indicating strong collinearity [14,15]. In cases of multicollinearity among variables, these variables were entered into different NARDL models alongside other meteorological drivers to investigate their effects on HFRS.

Autoregressive distributed lag (ARDL) model has been used to address issues related to autocorrelations and non-stationarity of key variables; details of this model have been provided in a prior study [16]. However, the ARDL model may yield biased results due to nonlinear and/or asymmetric impacts of meteorological factors on diseases [17]. The NARDL model was thus introduced to overcome the weakness. This approach allows for the investigation of both long- and short-term asymmetric dynamic effects [10,18]. In the presence of asymmetric impacts, the NARDL model can quantify the responses of HFRS to positive and negative changes in each of the meteorological factors by integrating the positive and negative partial sums of increments and decrements in these variables [10,18]. The NARDL analysis involves three steps [10,18,19]: First, investigation of the order of integration. The order of integration is not allowed to exceed one, although the NARDL model has relaxed this integration requirement. Besides, a pseudo regression may be generated by the non-stationary regressors. Thus, the augmented Dickey–Fuller (ADF) statistic was chosen to test the order of integration and stationarity in both independent and dependent variables [20]. Second, investigation of the long-term asymmetric cointegration. To determine whether a long-term asymmetric cointegration exists between regressors and dependent variables, the bounds

Table 1
Summary for monthly HFRS cases and weather factors in Shanxi, 2004–2019.

Variable	Mean	S.D.	Min	P_{25}	P_{50}	P_{75}	Max	VIF
HFRS cases	137.90	177.91	9.00	43.75	74.00	145.50	1209.00	–
MRH	64.74	9.93	42.24	58.14	63.89	72.00	84.76	5.97
AP	54.10	50.47	0.07	11.87	40.76	83.78	251.57	4.13
MT	12.23	9.08	−5.42	4.00	13.41	20.60	26.40	7.99
MWV	1.97	0.22	1.50	1.81	1.95	2.13	2.58	2.52
ASH	172.23	42.30	58.64	142.74	171.92	200.65	264.20	4.61
HFRS cases, 1-month lag	–	–	–	–	–	–	–	1.58

HFRS, hemorrhagic fever with renal syndrome; MRH, mean relative humidity; AP, aggregate precipitation; MT, mean temperature; MWV, mean wind velocity; ASH, aggregate sunshine hours, S.D., standard deviation; VIF, variance inflation factor.

test (F statistic) was applied [21]. If evidence suggests such a relationship is present, a Wald test is conducted to investigate short- and long-term asymmetries. Third, effect estimation. The positive and negative dynamic multiplier effects of regressors on the dependent variable are estimated accordingly.

Logarithmic transformation helps reduce the variation of dependent variables and better interpret the results, and thus the log(HFRS) was used in this study. The NARDL notation was below,

$$\Delta log(Y_t) = a_0 + \sum_{i=1}^{p_i} \varphi_i log(Y_{t-p_i}) + \sum_{i=0}^{q_1} \delta_{1i}^{+} x_{t-q_{1i}}^{+} + \sum_{i=0}^{q_2} \delta_{1i}^{-} x_{t-q_{2i}}^{-} + \sum_{i=1}^{p_2} p_{2i} \Delta log(Y_{t-p_{2i}}) + \sum_{i=0}^{q_3} \tau_{3i}^{+} \Delta x_{t-q_{3i}}^{+} \sum_{i=0}^{q_4} \tau_{4i}^{-} \Delta x_{t-q_{4i}}^{-} + a_1 month + \epsilon_t$$

where, Y_t represents the HFRS cases, x signifies the meteorological factors such as MRH, AP, MT, MWV, and ASH, x^+ and x^- are the positive and negative partial sums of increases and decreases in each meteorological factor, respectively, p and q denote the optimal lag orders of the HFRS cases and meteorological variables, respectively, δ_{1i}^{+} and δ_{1i}^{-} signify the long-term equilibrium parameters for the dependent variable, τ_{3i}^{+} and τ_{3i}^{-} refer to the short-term parameters for the dependent variable, month represents the seasonal variables, Δ refers to the first-order difference.

In this study, the maximum lag orders were set at four months, reflecting an approximate 16-week incubation period from HFRS infection to the onset of symptoms [22]. The optimal lag orders were then determined using various criteria, including the Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), Hannan-Quinn (HQ) criterion, log-likelihood, and adjusted R^2. To assess autocorrelation in the dependent variable, the partial autocorrelation function (PACF) was employed, which measures the correlation between current observations and past observations while controlling for other variables [23]. To account for seasonal effects, 11 monthly dummy variables were incorporated into the model. Furthermore, the stability of the NARDL model was evaluated using cumulative sum (CUSUM) and CUSUM of squares statistics [21]. All statistical analyses were conducted using EViews 10 (IHS, Inc. USA) and R 4.2.0 (R Development 164 Core Team, Vienna, Austria), with statistical significance defined as a two-sided $P \leq 0.05$.

3. Results

3.1. Statistical description

During 2004–2019, a total of 26,431 cases of HFRS were reported in Shaanxi, averaging 138 cases per month and approximately 1652 cases annually. Overall, the incidence of HFRS demonstrated a declining trend over this period (AAPC = -0.498 %, 95 %*CI* -13.247 % to 12.602 %), with the highest peak occurring in 2012, when 3591 cases were reported (9.482 cases per 100,000 people). Following this peak, the incidence steadily decreased until 2016, when only 933 cases were recorded (2.408 cases per 100,000 people). The incidence of HFRS exhibited clear seasonal and periodic patterns, with peaks typically observed in December and troughs in March each year.

A summary of monthly HFRS cases alongside relevant meteorological factors is provided in Table 1. The mean values of MRH, AP, MT, MWV, and ASH were 64.74 ± 9.93 %, 54.10 ± 50.47 mm, 12.23 ± 9.08 °C, 1.97 ± 0.22 m/s, and 172.23 ± 42.30 h, respectively. As illustrated in Fig. 1, there appears to be a similar trend between HFRS and MT, MWV, and ASH. In contrast, HFRS incidence showed an inverse relationship with MRH and AP. Importantly, no correlations exceeded 0.9, nor did any VIF values surpass 10 among the variables, indicating a lack of strong collinearity (Table 1 and Fig. 2).

3.2. Development of the NARDL and ADRL models

The ADF test indicated that both the dependent and independent variables were non-stationary, as evidenced by the following *P*-values: log(HFRS) ($P = 0.272$), MT ($P = 0.885$), ASH ($P = 0.387$), MWV ($P = 0.584$), AP ($P = 0.706$), and MRH ($P = 0.718$). However, after differencing the data once, all variables became stationary ($P < 0.001$). The PACF revealed significant autocorrelation at delays of one and two months (**Fig. S1**). Furthermore, the bounds test yielded an F of 6.735 (which far exceeded the critical values [$I_0 = 1.82$, $I_1 = 2.99$]), confirming the presence of a long-term asymmetric cointegration relationship among the variables. Lastly, a wide range of NARDL models were developed (**Table S1** and **Fig. S2**). Of the various candidates, we chose the NARDL(1, 4, 0, 4, 4, 0, 0, 2, 0, 4, 4) specification (in which the lag of log(HFRS) was one, lags of MRH(+) and MRH(−) were four and zero, respectively, lags of AP(+) and AP(−) were four, lags of MT(+) and MT(−) were zero, lags of MWV(+) and MWV(−) were two and zero, respectively) as the optimal model due to its lower AIC (0.372), BIC (1.132), and HQ (0.68), in conjunction with a higher adjusted R^2 value of 0.927 and a log-likelihood of 9.211. As shown in Fig. 3, the resulting residuals from the CUSUM and CUSUM of squares tests remained within the 95 % *CI*, substantiating the stability of the NARDL model. Likewise, the ARDL(1, 4, 3, 4, 2, 4) model was identified as the best specification among the possible ARDL candidates (**Table S2** and **Fig. S3**). Notably, the error metrics for NARDL—mean absolute error (MAE = 23.607) and root mean squared error (RMSE = 26.306)—were lower than those for ARDL (MAE = 24.986 and RMSE = 48.182). This suggests that the NARDL model provides a more accurate representation of the epidemic dynamics of HFRS by accounting for both long- and short-term asymmetries compared to the ARDL model (Fig. 4).

3.3. The asymmetric and symmetric effects of meteorological factors on HFRS

Based on the findings presented in Table 2, there was a statistically significant positive long-term relationship between AP and HFRS. Specifically, a 1 mm increase in AP was associated with an approximate 4.3 % rise in HFRS, while a 1 mm decrease in AP resulted in an approximately 3.7 % increase in HFRS, indicating a cumulative effect on HFRS incidence. Conversely, the long-term coefficients for MRH(−) were statistically significant but negatively correlated with HFRS; a 1 % decrease in MRH corresponded to an approximate 5.7 % reduction in HFRS. Meanwhile, MT, MWV, and ASH did not show significant long-term coefficient. In terms of short-term dynamics, ΔMWV(+) at a 1-month lag exhibited a substantial positive effect on HFRS, with an increase of 1 m/s in MWV leading to an approximate 83.4 % rise in HFRS. On the other hand, ΔMRH(+) at a 3-month lag, ΔAP(+) and ΔAP(−) at a 1-month lag, along with ΔASH(+) at a 1-month lag and ΔASH(−) at a 3-month lag, demonstrated a more pronounced negative short-term effect on HFRS. Specifically, when MRH, AP, and ASH increased by 1 %, 1 mm, and 1 h, HFRS increased approximately by 2.1 %, 1.0 %, and 0.5 %, respectively. Conversely, decreases in AP and ASH by 1 mm and 1 h

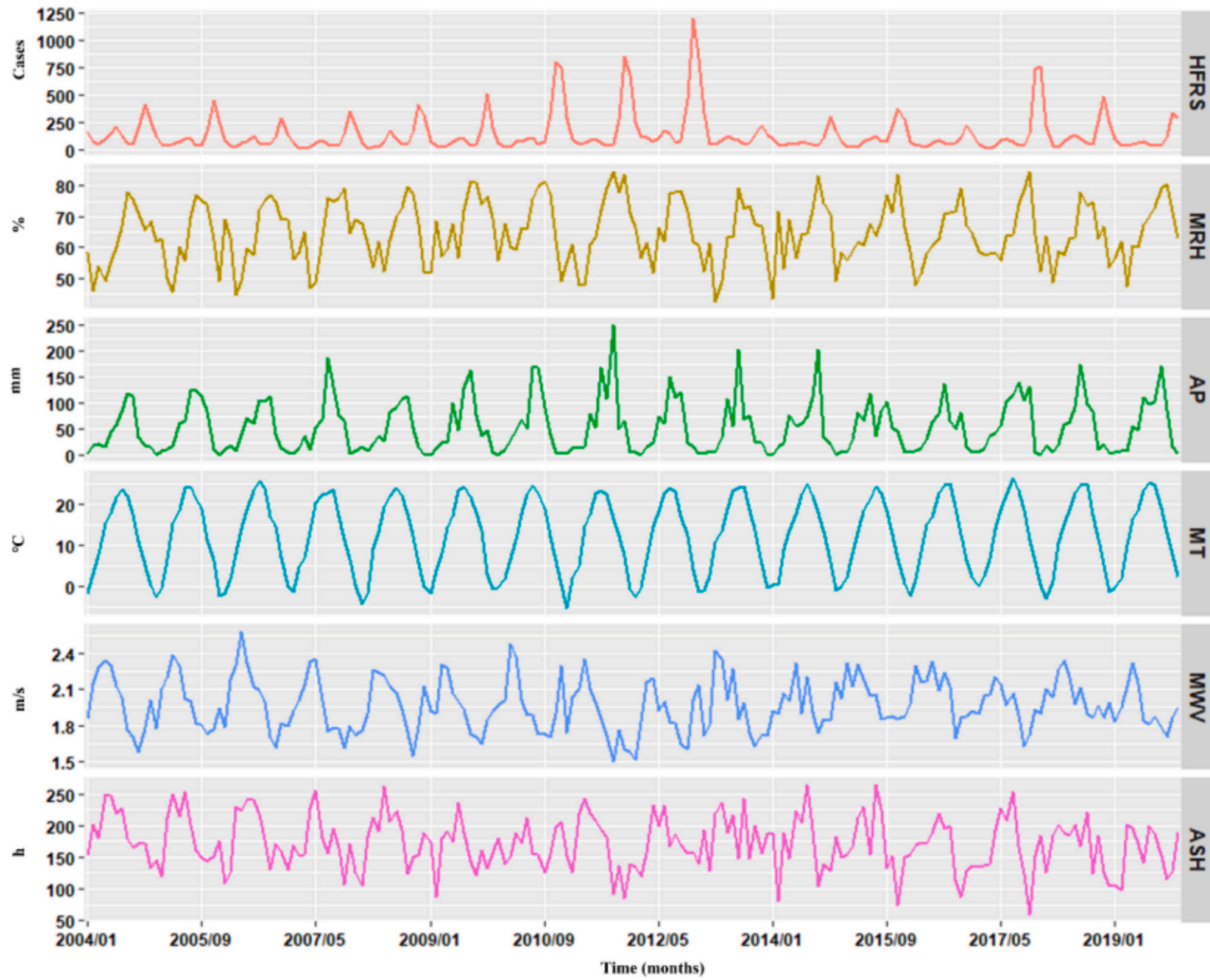

Fig. 1. Time series graph suggesting the changing patterns of the weather variables and HFRS cases in Shanxi, 2004–2019 (HFRS, hemorrhagic fever with renal syndrome; MRH, mean relative humidity; AP, aggregate precipitation; MT, mean temperature; MWV, mean wind velocity; ASH, aggregate sunshine hours).

resulted in increases in HFRS of about 1.0 % and 0.6 %, respectively. The Wald test results listed in Table 3 indicated potential long-term asymmetric impacts of AP and MWV on HFRS, a finding further supported by the dynamic multiplier plots shown in Figs. 5a-5f, despite the long-term coefficient for MWV being non-significant. No long-term asymmetric relationships were observed for MRH, MT, and ASH. However, both MWV and MRH may exert short-term asymmetric effects on HFRS. For instance, as illustrated in Fig. 5d, HFRS incidence rises gradually with increases in AP(+). In the short term, AP(−) initially elevates the incidence of HFRS before subsequently decreasing it; yet over the long term, the relationship between AP(−) and HFRS turns negative. Ultimately, considering the combined effects of fluctuations in AP(+) and AP(−), the overall impact leads to an increase in HFRS incidence.

4. Discussion

The relationship between human health, animal health, and the environment has never been more crucial than in the contemporary context of global health challenges. The One Health approach, an integrative framework that promotes a collaborative effort across various sectors, is essential for addressing health issues that transcend human, animal, and environmental domains [24]. By understanding the ecological dynamics that contribute to the transmission of HFRS, stakeholders can implement comprehensive strategies to prevent outbreaks, educate communities, and enhance disease management protocols. This study found that, from a long-term perspective, AP had a significant positive nonlinear association with HFRS. In the short term, ΔMWV(+) at a 1-month lag was positively associated with HFRS, while ΔMRH(+) at a 3-month lag, ΔAP(+) and ΔAP(−) at a 1-month lag, and ΔASH(+) at a 1-month lag and ΔASH(−) at a 3-month lag exhibit a reverse association with HFRS. This is the only study to investigate both long- and short-term asymmetric impacts of meteorological factors on HFRS using the NARDL model in Shaanxi. The ARDL model is widely used for its capacity to estimate long- and short-term relationships among time series data while accommodating various orders of integration [16]. In the context of meteorological factors influencing HFRS, the ARDL model can reveal fundamental associations; however, it often operates under the assumption of linear impacts across the variables involved. This assumption may oversimplify the actual dynamics, as real-world relationships between meteorological variables and disease incidence may exhibit nonlinearity and asymmetry [10]. In contrast, the NARDL model expands upon the ARDL framework by allowing for nonlinear interactions among variables [10]. It enables researchers to differentiate the impact of positive and negative changes in explanatory variables, thus offering a more nuanced view of how meteorological factors affect the incidence of HFRS. By distinguishing between these dimensions, the NARDL model can reveal potentially critical insights into the underlying mechanisms driving the association between climate variables and disease outcomes. Our results also corroborate the lead time and both asymmetric and symmetric impacts of meteorological

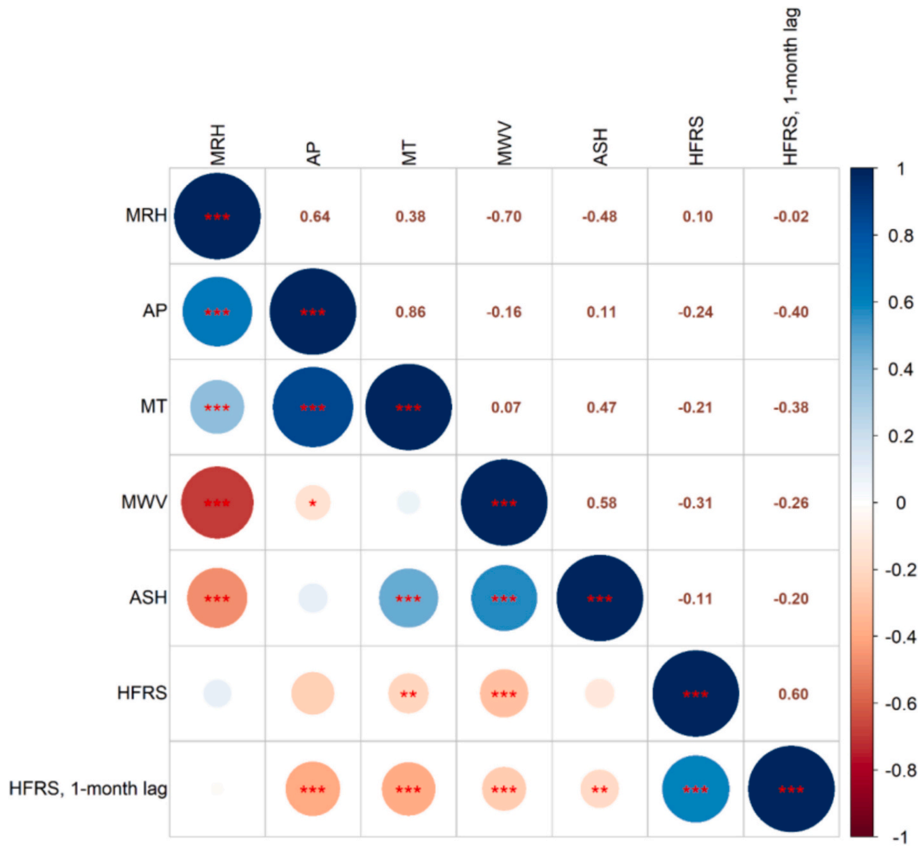

Fig. 2. Spearman's correlation between variables. It was observed that there was no correlation greater than 0.9 between variables, indicating an absence of strong collinearity between variables (HFRS, hemorrhagic fever with renal syndrome; MRH, mean relative humidity; AP, aggregate precipitation; MT, mean temperature; MWV, mean wind velocity; ASH, aggregate sunshine hours).

parameters on HFRS, highlighting the usefulness of the NARDL model in capturing the dynamic epidemic structure of HFRS incidence. These findings are helpful in estimating HFRS epidemics, providing sufficient lead time to develop targeted policies and implement effective public health interventions.

Our results revealed that overall a decreasing trend was observed in HFRS incidence, consistent with global and national epidemic patterns in China [3]. This decline can be attributed to a confluence of factors, including improved public health interventions, enhanced agricultural practices, increased public awareness, and ecological modifications [25]. As China continues to develop and implement comprehensive strategies for the prevention and control of HFRS, it is imperative that these efforts remain multifaceted, integrating education, community engagement, vaccination campaigns, and environmental management [25]. While the current trend is encouraging, maintaining vigilance is essential to preserve these gains and protect vulnerable populations from potential outbreaks of HFRS, as changing ecological conditions and patterns of human behavior could pose new challenges in the future [25–27]. Besides, our findings revealed a distinct seasonal profile in HFRS morbidity, with peaks in December and troughs in March, in alignment with the seasonality across China [4]. This pronounced seasonal profile may be closely linked to variations in rodent density and rainfall, both of which exhibit seasonal fluctuations [28].

An intriguing finding is that AP was one of the most important contributors to HFRS, exhibiting a notable positive long-term effect on HFRS, and it seems that an increase in AP has a stronger effect than a reduction, indicating an asymmetric relationship. Conversely, a significant negative short-term effect of AP was observed at 1-month, 2-month, and 3-month lags. Low-lying regions and wetlands with moist soil serve as ideal habitats, heightening the risk of HFRS transmission [29]. Moist and semi-moist soil is essential for the growth of vegetation and crops that either directly or indirectly provide sustenance for rodent hosts, resulting in larger rodent populations [30,31]. The densities of hosts, particularly hantavirus-positive hosts, were positively correlated with the risk of HFRS transmission [32]. Additionally, the previously mentioned significant negative short-term effect of AP at 1-month, 2-month, and 3-month lags suggests that excessive precipitation may disrupt the nests of host animals, thereby reducing the likelihood of rodent-rodent contact, rodent-human interaction, and subsequent virus transmission [12,29,33].

The second important finding is that MRH(−) had a negative long-term effect on HFRS, indicating an approximate 5.7 % decrease in HFRS incidence with a 1 % reduction in MRH. This aligns well with several studies that have reported a positive association between MRH and HFRS [17,30,34]. Moisture not only influences the growth of food sources that determine rodent population size, thereby affecting the HFRS transmission, but also directly influences rodent activity and hantavirus infectivity [35]. However, contrary to our conclusions, several studies reported a positive relationship between MRH and HFRS [22,36,37]. This discrepancy may be attributed, in part, to the different models employed in data analysis, variations in geographic regions, or the absence of autoregressive adjustments in the dependent variable.

The third important finding is that MWV had a positive short-term asymmetric impact on HFRS, and unfortunately the long-term coefficient was non-significant. This was consistent with the previous studies in Changchun, Shenyang, and Heilongjiang [12,38,39]. The short-term positive impact of wind on HFRS transmission involves two main mechanisms: increased human exposure to infectious materials and changes in rodent behavior [27,36,40]. First, high winds can aerosolize rodent urine and droppings, elevating the concentration of viral particles in the air and exposing humans during outdoor activities. Second, wind prompts rodents to seek shelter, but this behavior can drive them

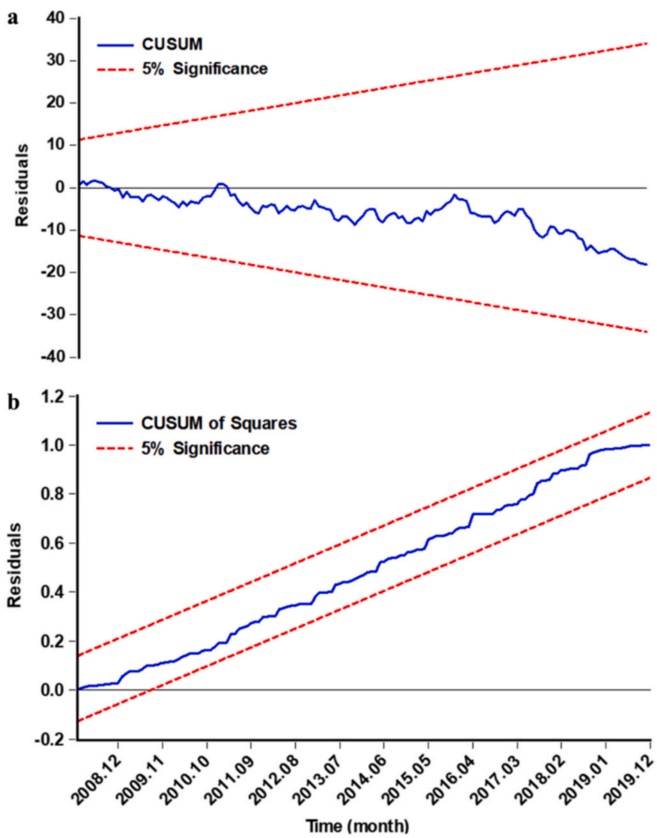

Fig. 3. Stability test for the nonlinear autoregressive distributed lag model (NARDL). a. Cumulative sum (CUSUM) test, b. CUSUM of squares test. The CUSUM and CUSUM of squares were within 95 % confidence interval (CI) at different time confirmed the validity and stability of the NARDL.

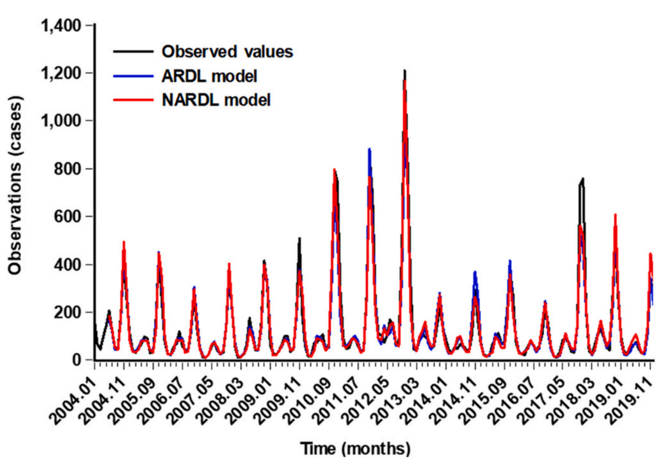

Fig. 4. Comparison of the forecasts under the nonlinear autoregressive distributed lag (NARDL) and autoregressive distributed lag (ARDL) models with the observed values. It seemed that the forecasts could be closer to the trend and seasonality under the NARDL model than under the ARDL model.

into areas with more human interaction, such as residential regions or agricultural fields. This increases the likelihood of zoonotic spillover events. Third, wind may also worsen drought conditions, affecting food supplies for rodents and forcing them closer to human settlements. The resultant increase in rodent-human interactions forms a nexus where the risks of HFRS transmission escalate. Lastly, Shaanxi is a windy province, strong winds can disrupt rodent populations, causing temporary population fluctuations as they disperse and settle in new areas, further

Table 2
Long- and short-term effects by use of the optimal NARDL and ARDL.

NARDL			ARDL		
Variable	Coefficient	*P*	Variable	Coefficient	*P*
Long-run effect			Long-run effect		
MRH(+)	−0.025	0.327	MRH	0.034	0.213
MRH(−)	−0.057	0.040	AP	0.029	0.010
AP(+)	0.043	<0.001	MT	−0.106	0.472
AP(−)	0.037	<0.001	MWV	−0.316	0.781
MT(+)	0.083	0.262	ASH	0.012	0.109
MT(−)	0.069	0.365	Short-run effect		
MWV(+)	−1.442	0.223	ΔMRH	−0.015	0.014
MWV(−)	1.022	0.348	ΔMRH, 1-month lag	−0.017	0.029
ASH(+)	0.009	0.273	ΔMRH, 2-month lag	−0.016	0.036
ASH(−)	0.013	0.119	ΔMRH, 3-month lag	−0.016	0.007
Short-run effect			ΔAP	−0.001	0.315
ΔMRH(+)	−0.016	0.074	ΔAP, 1-month lag	−0.005	<0.001
ΔMRH(+), 1-month lag	−0.004	0.636	ΔAP, 2-month lag	−0.003	0.004
ΔMRH(+), 2-month lag	−0.006	0.471	ΔMT	0.020	0.297
ΔMRH(+), 3-month lag	−0.021	0.007	ΔMT, 1-month lag	0.025	0.340
ΔAP(+)	0.001	0.314	ΔMT, 2-month lag	0.027	0.241
ΔAP(+), 1-month lag	−0.012	<0.001	ΔMT, 3-month lag	0.047	0.011
ΔAP(+), 2-month lag	−0.010	<0.001	ΔMWV	0.324	0.076
ΔAP(+), 3-month lag	−0.003	0.087	ΔMWV, 1-month lag	0.616	0.001
ΔAP(−)	−0.003	0.036	ΔASH	−0.003	0.017
ΔAP(−), 1-month lag	−0.010	<0.001	ΔASH, 1-month lag	−0.004	0.020
ΔAP(−), 2-month lag	−0.005	0.001	ΔASH, 2-month lag	−0.004	0.010
ΔAP(−), 3-month lag	−0.002	0.028	ΔASH, 3-month lag	−0.004	0.003
ΔMWV(+)	0.436	0.089			
ΔMWV(+), 1-month lag	0.834	0.002			
ΔASH(+)	−0.002	0.202			
ΔASH(+), 1-month lag	−0.005	0.006			
ΔASH(+), 2-month lag	−0.004	0.005			
ΔASH(+), 3-month lag	−0.002	0.096			
ΔASH(−)	−0.003	0.045			
ΔASH(−), 1-month lag	−0.004	0.097			
ΔASH(−), 2-month lag	−0.005	0.013			
ΔASH(−), 3-month lag	−0.006	<0.001			

Note, adjustment for seasonality as dummy variable. NARDL, nonlinear autoregressive distributed lag; ARDL, autoregressive distributed lag; MRH, mean relative humidity; AP, aggregate precipitation; MT, mean temperature; MWV, mean wind velocity; ASH, aggregate sunshine hours, S.D., standard deviation; VIF, variance inflation factor.

heightening the potential for human encounters.

Our study documented negative short-term associations of ASH(+) and ASH(−) with HFRS, with significant association coefficients observed at delays of 1–3 months. However, the lack of evidence for asymmetry and the extremely small coefficient values indicate a very weak short-term relationship. Previous research has also reported negative associations between sunshine hours and HFRS incidence [33,39]. Sunshine hours and wind speed could influence crop yield, rodent reproduction, and vector density, which in turn may affect the

Table 3
Wald test results for Long- and short-term asymmetries.

Variable	Long-term asymmetry		Short-term asymmetry	
	WLT	*P*	WST	*P*
MT	0.646	0.422	–	–
AP	9.072	0.003	0.157	0.692
ASH	2.015	0.156	1.528	0.216
MWV	10.735	0.001	10.318	0.001
MRH	3.067	0.080	5.978	0.015

MRH, mean relative humidity; AP, aggregate precipitation; MT, mean temperature; MWV, mean wind velocity; ASH, aggregate sunshine hours, S.D., standard deviation; VIF, variance inflation factor; WLT, Wald long-term symmetry; WST, Wald short-term symmetry.

likelihood of HFRS occurrence [17]. A deeper investigation into the plausible mechanism underlying the relationship between ASH and HFRS is warranted. In addition, researchers have identified both positive and negative associations between AT and HFRS incidence [4,34,41], while our study found no significant long-term or short-term relationships in this regard. Our study uses the NARDL model, which provides an insight into the link between variables by decomposing the effect of regressors into short- and long-term components—a capability that current models, aside from NARDL, do not provide. Consequently, we expect further validation efforts to be conducted in other areas.

Our research specifically focused on the asymmetric and/or symmetric impacts of variations in meteorological factors on HFRS incidence in both the long and short term. Prior study has emphasized the significance of considering the changes in population immunity, autocorrelations, possible lags and relationship patterns, and seasonality when performing time series analyses [42]. Although we did account for most of these factors, changes in population immunity could not be addressed due to a lack of data. Therefore, we are confident that our findings provide valid and reliable evidence that variations in meteorological factors play a crucial asymmetric and/or symmetric role in influencing HFRS incidence in both the long and short term. Nonetheless, our study has some limitations. First, under-reporting or under-

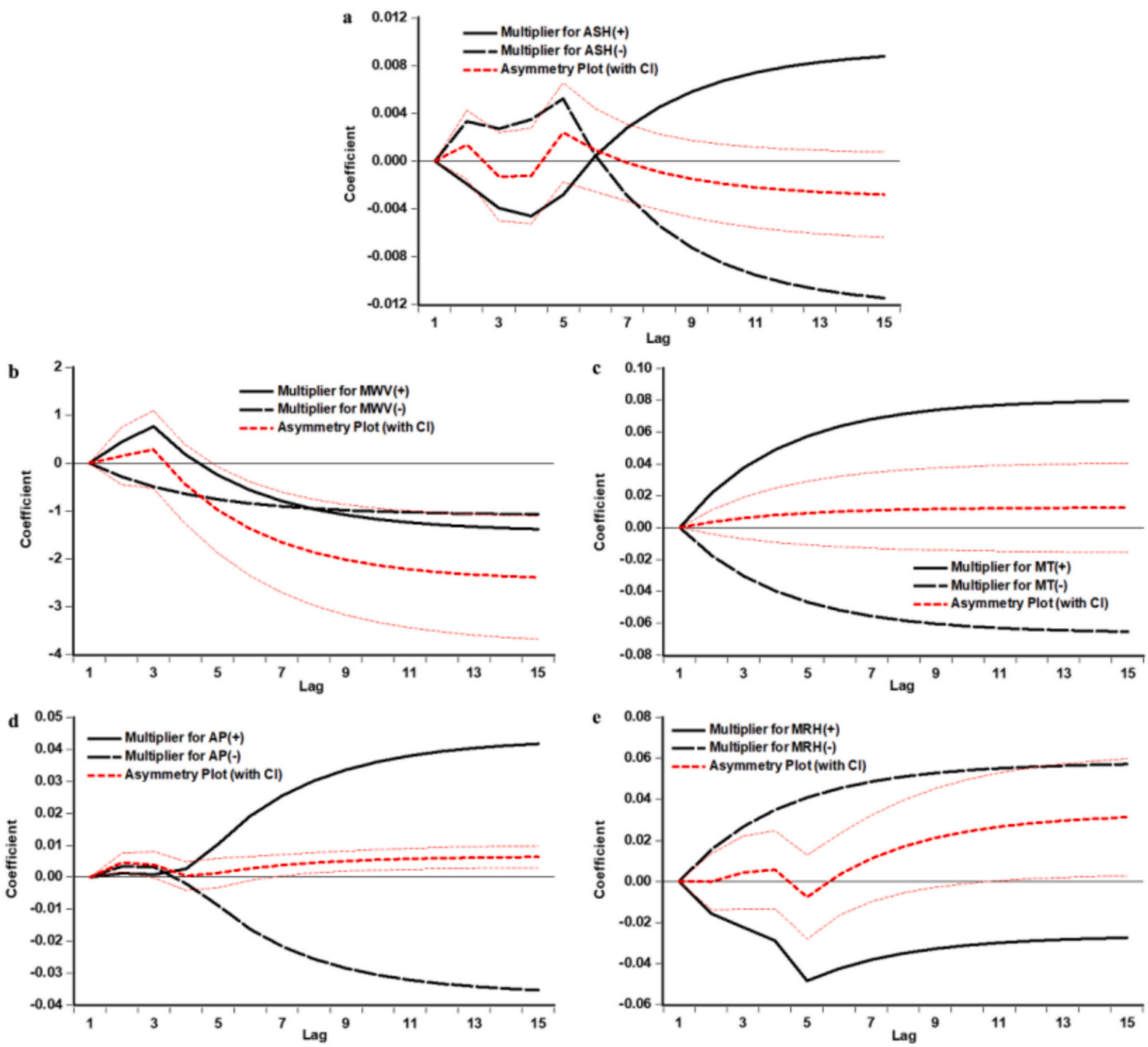

Fig. 5. Dynamic multiplier asymmetric effects of weather factors on hemorrhagic fever with renal syndrome (HFRS). a. multiplier graph for aggregate sunshine hours (ASH), b. multiplier graph for mean wind velocity (MWV), c. multiplier graph for mean temperature (MT), d. multiplier graph for aggregate precipitation (AP), e. multiplier graph for mean relative humidity (MRH).

diagnosis is an unavoidable issue in a passive monitoring system. Second, this ecological trend study does not permit an examination of individual-based relationships or the inference of causal effects. Third, daily or weekly data could offer deeper insights into temporal differences across years; however, their unavailability limits further investigation. Finally, we did not control for the effects of the unmeasured confounders (e.g., geographic and socioeconomic factors, population density, and host susceptibility).

5. Conclusion

Our study elucidates the significant long- and short-term asymmetric and symmetric contributions of AP, MWV, MRH, and ASH to the HFRS incidence through a 16-year ecological trend study. Given the implications of global climate change, it is imperative that meteorological variables are integrated into strategies for the control and prevention of HFRS. By understanding the ecological dynamics that facilitate the transmission of hantaviruses, stakeholders can implement comprehensive strategies for outbreak prevention, community education, and enhancement of disease management protocols. As an infectious disease continues to pose significant threats to global health, the necessity for multidisciplinary cooperation in understanding and mitigating these risks has never been more apparent. Embracing the One Health paradigm is not only critical for managing HFRS but is also essential for fortifying overall public health resilience against future zoonotic threats.

Ethics approval and consent to participate

This study protocol was approved by the study institutional review board of Xinxiang Medical University (No: XYLL-2019072). Because the DCPHS system shares the monthly number of HFRS cases anonymously and we cannot access any identifying information of the patients, and hence informed consent was waived.

Consent for publication

Not applicable.

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CRediT authorship contribution statement

Chenlu Xue: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Bingjie Zhang:** Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Writing – original draft, Writing – review & editing. **Yanyan Li:** Formal analysis, Investigation, Software, Validation, Writing – original draft, Writing – review & editing. **Xinxiao Li:** Formal analysis, Investigation, Validation, Writing – review & editing. **Chunjie Xu:** Conceptualization, Data curation, Formal analysis, Investigation, Validation, Visualization, Writing – original draft, Writing – review & editing. **Yongbin Wang:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

All data for this work are presented in the results and conclusions or please contact the corresponding author on the reproducibility of this work.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.onehlt.2024.100895.

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