Quality Improvement Study

Medicine®

OPEN

Evaluation of the effectiveness of a pilot study of hospital-based hepatitis C epidemic surveillance

Dongxian Ye, MD[a], Yuqing Tang, MD[b], Yuanliang Gu, MD[a], Harris Haleem, MD[b], Libo Zhang, MD[a], Youping Zhang, MD[a], Chunxia Xu, MD[a,*], Jinshun Zhao, PhD[b,*]

Abstract

The aim of this study was to evaluate the effectiveness of hospital-based hepatitis C epidemic surveillance initiated by China's CDC STD/AIDS (National Center for AIDS/STD Control and Prevention of Chinese Center for Disease Control and Prevention) Prevention and Control Center in 2017.

A total of 104,666 anti-hepatitis C virus (HCV) and 633 HCV-RNA detection records in our hospital from 2014 to 2017 were used to analyze the anti-HCV and HCV-RNA detection rates and positive rates in patients before and after implementation of epidemic surveillance.

We found that the estimated HCV positive rate was 0.395% in all patients, and this rate increased to 0.533% after the pilot research. The positive rates of anti-HCV were significantly enhanced, although certain differences were observed among different departments. Significant increase of positive rate of HCV-RNA was only found in the inpatients from nonsurgical departments. Eighty-one cases were diagnosed after this pilot research, exceeding the 70 total cases in the previous 3 years. Most cases were diagnosed by nonsurgical departments; the upward trend of the cases diagnosed by surgical departments cannot be ignored.

Our study indicates expanding anti-HCV and HCV-RNA detection in the target populations in hospitals is a useful strategy for finding more occult HCV infection. In addition, our results provide useful pilot data of the seroepidemiology of Hepatitis C for the special populations in hospitals, which will provide valuable information for public health research.

Abbreviations: ALT = alanine aminotransferase, HCV = hepatitis C virus, IgG = immunoglobulin G, OD = optical density, WHO = World Health Organization.

Keywords: effectiveness evaluation, epidemic surveillance, hepatitis C, hospital-based, seroepidemiology

1. Introduction

Hepatitis C is a global epidemic caused by the hepatitis C virus (HCV) and mainly transmitted by blood. Because of the virus's atypical symptoms,[1] most cases of hepatitis C are misdiagnosed or missed altogether. If not treated at early stage of infection, about 20% to 30% of patients with hepatitis C may develop into liver fibrosis and cirrhosis[2,3]; more than 20% of patients with cirrhosis will eventually develop liver cancer.[4–6] Therefore, early diagnosis of hepatitis C is particularly important for medical intervention.[7] HCV antibody and RNA detection are normally used to screen and diagnose early HCV infection. Mohd Hanafiah et al[8] reported that the global rate of anti-HCV-positive cases increased steadily from 2.3% in 1990 to 2.2% in 2005. The latest data from the World Health Organization (WHO) show that the anti-HCV-positive rate in developed countries is 0.2% to 2.2% but is nearly 7% in developing countries. According to this estimation, around 170 million people are infected with HCV worldwide.[8,9] In 1992, in China, the rate of anti-HCV-positive cases was 3.20%, equating to an estimated 40 million people infected with HCV.[10] But the reported positive rate of anti-HCV in China decreased to 0.43% in 2006[11,12]; in eastern China, this rate decreased to 0.37%,[11] which is even lower than the infection rate of developing countries published by WHO.[13] Based on the above rates, an estimated 5.6 million people are infected with hepatitis C in China, suggesting that China has a low incidence of HCV infection.[14] However, many epidemiology scientists have questioned this conclusion; therefore, an update of national serological data of hepatitis C is urgent in China.[14]

To explore the effectiveness of anti-HCV and HCV-RNA detection in the expanding target population, China's CDC STD/AIDS (National Center for AIDS/STD Control and Prevention of Chinese Center for Disease Control and Prevention) Prevention and Control Center organized 20 hospitals in 2017 from 7 different provinces for a pilot study of hospital-based hepatitis

Editor: Oliver Schildgen.

DY and YT contributed equally to this study.

This work was supported by the pilot research on hospital-based Hepatitis C epidemic surveillance conducted by China's CDC STD/AIDS Prevention and Control Center.

The authors report no conflicts of interest.

[a] Department of Prevention and Health Care, Beilun Branch of the First Affiliated Hospital, College of Medicine, Zhejiang University, [b] Department of Preventative Medicine, Zhejiang Provincial Key Laboratory of Pathological and Physiological Technology, School of Medicine, Ningbo University, Ningbo, Zhejiang, P.R. China.

[*] Correspondence: Chunxia Xu, Department of Prevention and Health Care, Beilun Branch of the First Affiliated Hospital, College of Medicine, Zhejiang University, Ningbo, Zhejiang 315800, P.R. China (e-mail: 160413343@qq.com); Jinshun Zhao, Ningbo University Medical School, Ningbo, Zhejiang Province 315211, China (e-mail: zhaojinshun@nbu.edu.cn).

How to cite this article: Ye D, Tang Y, Gu Y, Haleem H, Zhang L, Zhang Y, Xu C, Zhao J. Evaluation of the effectiveness of a pilot study of hospital-based hepatitis C epidemic surveillance. Medicine 2019;98:51(e18334).

Received: 28 August 2019 / Received in final form: 21 October 2019 / Accepted: 12 November 2019

http://dx.doi.org/10.1097/MD.0000000000018334

C epidemic surveillance. Beilun Branch of the First Affiliated Hospital, College of Medicine, Zhejiang University, which provides medical services for more than 300,000 inhabitants and 600,000 floating populations and has an average of 1.3 million outpatients and 30,000 inpatients per year, was selected as one of the participants. The purpose of this study was to help search for an efficient strategy to find more occult HCV infection cases as well as an effective method to survey the infection rate in the target hospital-based populations.

2. Materials and methods

The study was approved by the Ethics Committee of the College of Medicine, Zhejiang University. All procedures were in accordance with the ethical standards of the Helsinki Declaration. Data were collected as part of public health surveillance, and individual patient consent was required before obtaining the patient's biological specimen. All identifiable patient-level data were anonymous.

2.1. Target populations for expanded screening for HCV infection

In this study, patients belonging to the following populations were screened for the HCV (These criteria apply to all-patients):

Individuals with a high risk of HCV infection include: a history of intravenous-drug abuse; a history of needle stick injuries caused by occupational or other reasons (tattoos, perforations, acupuncture therapy, and so on); a history of iatrogenic exposure such as surgery, dialysis, unsanitary dental procedures, or organ/tissue transplants; a history of high-risk sexual behavior such as sex with multiple partners and gay men; the sexual partners or family members of HCV patients; HIV-infected persons and their sexual partners; the infants of HCV-infected mothers for whom anti-HCV should be detected at 18 months after birth or HCV-RNA at 1 month after birth; persons with damaged skin and mucous membranes contaminated by the blood of HCV-infected persons; persons with a history of transfusion of blood and blood products (mainly before 1993).

The individuals with a high risk of HCV infection should be screened for HCV including a history of intravenous-drug abuse; a history of needle stick injuries caused by occupational or other reasons (tattoos, perforations, acupuncture therapy, etc.); a history of iatrogenic exposure such as surgery, dialysis, unsanitary dental procedures or organ/tissue transplants; a history of high-risk sexual behavior such as sex with multiple partners or gay men or HCV patients; a history of transfusion of blood and blood products (mainly before 1993). The infants from HCV-infected mothers should be detected anti-HCV at 18 months or HCV-RNA at 1 month after birth. The patients with damaged skin and mucous membranes contaminated by the blood of HCV-infected persons also should received the screening.

The individuals those are ready to carry out certain special or invasive operations should be screened for HCV including hemodialysis;a transfusion of blood and blood products; an invasive catheter implantation; an endoscopy implantation such as gastroscope, colonoscopy, bronchoscopy, cystoscopy.

The individuals with abnormal liver function such as elevated alanine aminotransferase (ALT) or bilirubin should be alsoscreened for HCV.

All these target populations, who are at high risk of HCV infection, were asked to be screened as early as possible. The detailed recommended processes for HCV screening are shown in Figure 1.

2.2. Criteria for diagnosis of hepatitis C

Hepatitis C was diagnosed according to epidemiological history, clinical manifestations and biochemical indicators. Clinically diagnosed cases were anti-HCV-positive patients who also had an epidemiological history and clinical manifestations or abnormal liver biochemical tests. Confirmed cases were those patients found to be HCV-RNA-positive. Acute and chronic HCV infections were distinguished according to the duration of the infection—$\leq$6 months for acute cases, and >6 months for chronic cases (Fig. 1).

2.3. Screening process of HCV

Anti-HCV detection was performed in the target populations. HCV-RNA detection was used to confirm that anti-HCV-positive individuals had an active HCV infection. If the physician was highly suspicious of the risk of HCV infection, HCV-RNA detection was also performed even if the anti-HCV result was negative (Fig. 1) because a false-negative for anti-HCV may exist due to severe immunodeficiency caused by HIV infections, organ-transplant, hypogammaglobulinemia, hemodialysis, and so on.

2.4. Detection methods for anti-HCV and HCV-RNA

All sera were analyzed using an anti-HCV reagent from Shanghai Kehua Bioengineering Co., Ltd. (Shanghai, China) for the detection of immunoglobulin G (IgG) antibodies to the HCV. The anti-HCV screening assay was performed according to the manufacturer's instructions. The results were determined by the optical density (OD) value of each well measured by a microplate reader (TECAN, Swiss) at 450 nm. The critical value (COV) was the average OD value of positive control $\times$10% + average OD value of negative control. If the sample's OD value/COV $\geq$1.0, the result was positive; otherwise, it was negative. The molecular HCV RNA assay is a confirmatory test using an HCV-RNA reagent from Shengxiang Biotechnology Co., Ltd. (Hunan, China). The RNA was extracted from serum samples using a spin column method, and the HCV-RNA assay was performed according to the manufacturer's instructions. ABI7500 real-time analysis (ABI) was used for reverse transcription-polymerase chain reaction analysis.

2.5. Statistical analysis

All anti-HCV, HCV-RNA, and corresponding clinical data were provided by a diagnostic laboratory department, which analyzed 104,666 anti-HCV detection records and 633 HCV-RNA detection records obtained in Beilun Branch of the First Affiliated Hospital, College of Medicine, Zhejiang University from January 2014 to December 2017. The statistical analyses were conducted using χ^2 tests as implemented in SPSS (version 13.0) (SPSS Inc, Chicago, IL). A P value of $\leq$.05 was considered statistically significant.

3. Results

3.1. Detection and positive rates of anti-HCV in outpatients and inpatients from 2014 to 2017

Although the yearly detection rates of anti-HCV in outpatients and inpatients had no significant difference from 2014 to 2017, the yearly positive rates of anti-HCV in both outpatients and inpatients showed an upward trend from 2014 to 2017. After the current project was implemented in 2017, the positive rates of

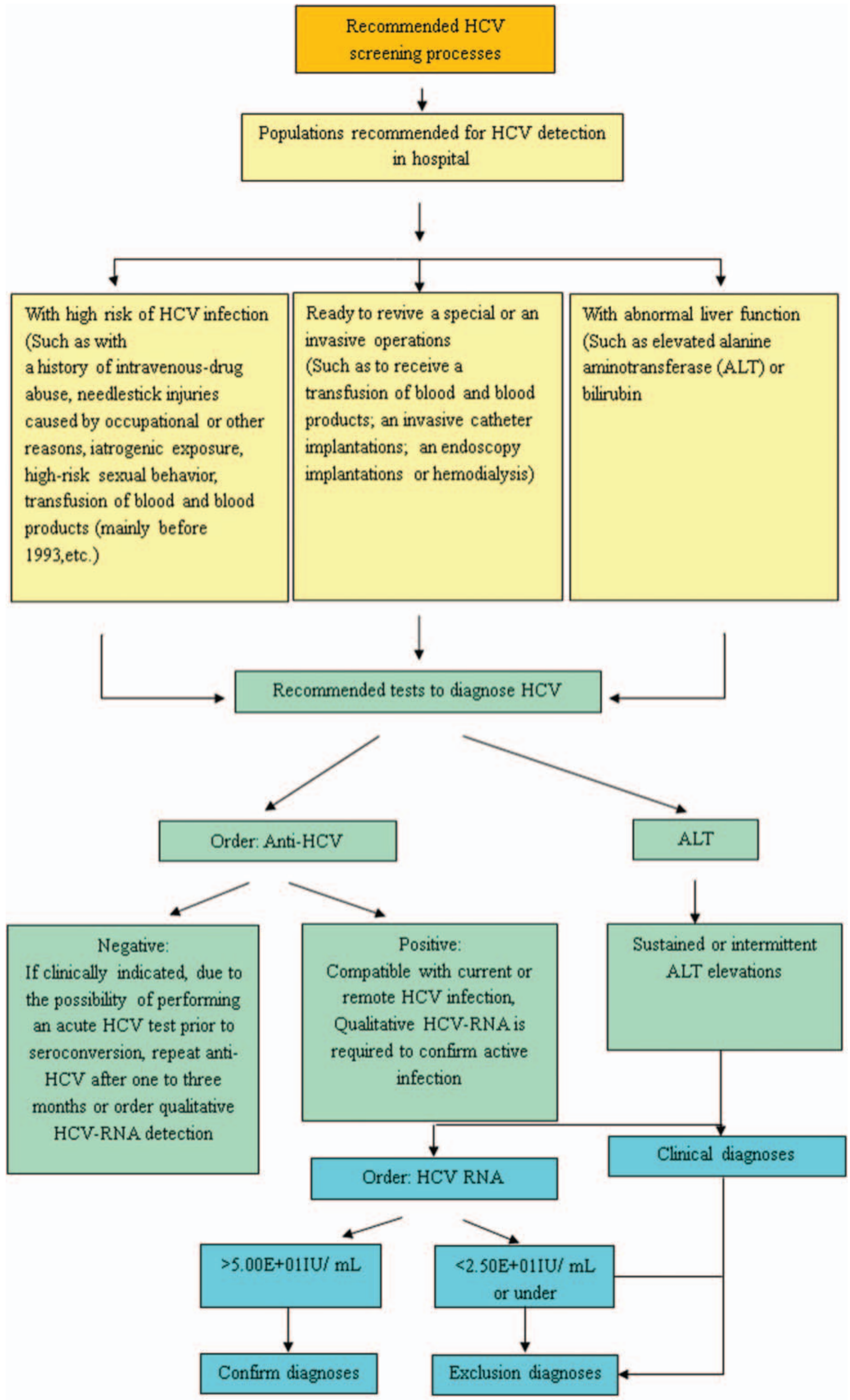

Figure 1. The flow-chart for the recommended HCV screening processes for the special populations in hospitals. HCV = hepatitis C virus.

anti-HCV in both outpatients and inpatients were significantly higher ($P<.01$) (Table 1).

Significant differences were found among different clinical departments. The positive rates of anti-HCV in nonsurgical departments were significantly higher for both outpatients and inpatients compared to surgical departments ($P<.01$). The overall positive rate of anti-HCV in nonsurgical departments was also significantly higher than that of surgical departments ($P<.01$). After the project was implemented in 2017, the positive rates of anti-HCV in outpatients and inpatients from surgical and nonsurgical departments were all enhanced significantly compared to the previous 3 years ($P<.01$) (Table 2).

Table 1

The detection and positive rates of anti-HCV in outpatients and inpatients from 2014 to 2017.

	Outpatients			Inpatients			Outpatients + inpatients		
Year	Cases	Detection cases, rate (%)	Positive cases, rate (%)	Cases	Detection cases, rate (%)	Positive cases, rate (%)	Cases	Detection cases, rate (%)	Positive cases, rate (%)
2014	1,232,781	7764 (0.630)	41 (0.528)	27,419	15,158 (55.283)	30 (0.198)*	1,260,200	22,922 (1.819)	71 (0.310)
2015	1,252,045	6997 (0.559)	44 (0.629)	28,908	16,405 (56.749)	32 (0.195)*	1,280,953	23,402 (1.827)	76 (0.325)
2016	1,316,167	7072 (0.537)	52 (0.735)	32,574	19,305 (59.265)	47 (0.243)*	1,348,741	26,377 (1.956)	99 (0.375)
2017	1,419,673	8853 (0.624)	74 (0.836)†	35,810	21,374 (59.687)	87 (0.407)‡,*	1,455,483	30,227 (2.077)	161 (0.533)§
Total	5,220,666	30,686 (0.588)	211 (0.688)	124,711	72,242 (57.928)	196 (0.271)*	5,345,377	102,928 (1.926)	407 (0.395)

Note: linear χ^2 test.
χ^2 test.
* $P<.01$, compared with outpatients.
† $P<.01$, compared with the previous 3 years.
‡ $P<.01$, compared with the previous 3 years.
§ $P<.01$, compared with the previous 3 years.

Table 2

The positive rates of anti-HCV in outpatients and inpatients from different clinical departments from 2014 to 2017.

	Outpatients				Inpatients				Outpatients + inpatients			
	Surgical departments		Nonsurgical departments		Surgical departments		Nonsurgical departments		Surgical departments		Nonsurgical departments	
Depart-ments	Detection cases	Positive cases, rate (%)	Detection cases	Positive cases, rate (%)	Detection cases	Positive cases, rate (%)	Detection cases	Positive cases, rate (%)	Detection cases	Positive cases, rate (%)	Detection cases	Positive cases, rate (%)
2014	4614	5 (0.108)	3150	36 (1.143)*	11297	14 (0.124)	3861	16 (0.414)*	15911	19 (0.119)	7011	52 (0.742)*
2015	3757	6 (0.160)	3240	38 (1.173)*	12136	21 (0.173)	4269	11 (0.258)*	15893	27 (0.170)	7509	49 (0.653)*
2016	3577	5 (0.140)	3495	47 (1.345)*	13931	29 (0.208)	5374	18 (0.335)*	17508	34 (0.194)	8869	65 (0.733)*
2017	4411	8 (0.181)	4442	66 (1.486)†,*	15131	48 (0.317)‡	6243	39 (0.625)§,*	19542	56 (0.287)‖	10685	105 (0.983)¶,*
Total	16359	24 (0.147)	14327	187 (1.305)*	52495	112 (0.213)	19747	84 (0.425)*	68854	136 (0.198)	34074	271 (0.795)*

Note: linear χ^2 test.
χ^2 test.
* $P<.01$, compared with surgical department.
† $P<.01$, compared with the previous 3 years.
‡ $P<.01$, compared with the previous 3 years.
§ $P<.01$, compared with the previous 3 years.
‖ $P<.01$, compared with the previous 3 years.
¶ $P<.01$, compared with the previous 3 years.

3.2. Detection and positive rates of HCV RNA in outpatients and inpatients from 2014 to 2017

No significant difference in detection and positive rates of HCV-RNA was found in outpatients and inpatients among different years (Table 3).

The positive rate of HCV-RNA in inpatients (47.154%) was almost twice as much as that in outpatients (24.706%). After implementation of the project, the detection rate of HCV-RNA in the anti-HCV-positive cases was enhanced to 88.820%, which was significantly higher than that of the previous 3 years (Table 3).

Significant differences were observed in the positive rates of HCV-RNA between surgical and nonsurgical departments. The positive rate of HCV-RNA in outpatients of nonsurgical departments was significantly higher compared to surgical departments. However, the positive rate of HCV-RNA in inpatients of nonsurgical departments was lower than that of surgical departments ($P<.01$). After implementation of the project in 2017, the

Table 3

The detection and positive rates of HCV RNA detection in different patients from 2014 to 2017.

	Outpatients			Inpatients			Outpatients+ inpatients			Anti-HCV-positive cases		
Year	Cases	Detection cases, rate (%)	Positive cases, rate (%)	Cases	Detection cases, rate (%)	Positive cases, rate (%)	Cases	Detection cases, rate (%)	Positive cases, rate (%)	Cases	Detection cases, rate (%)	Positive cases, rate (%)
2014	1,232,781	78 (0.006)	21 (26.923)	27,419	17 (0.062)	8 (47.059)*	1,260,200	95 (0.008)	29 (30.526)	71	42 (59.155)	15 (35.714)
2015	1,252,045	111 (0.009)	26 (23.423)	28,908	29 (0.100)	12 (41.379)*	1,280,953	140 (0.011)	38 (27.143)	76	36 (47.368)	16 (44.444)
2016	1,316,167	134 (0.010)	30 (22.388)	32,574	24 (0.074)	11 (45.833)*	1,348,741	158 (0.012)	41 (25.949)	99	57 (57.576)	22 (38.596)
2017	1,419,673	187 (0.013)	49 (26.203)	35,810	53 (0.148)	27 (50.943)†,*	1,455,483	240 (0.016)	76 (31.667)	161	143 (88.820)‡	65 (45.455)
Total	5,220,666	510 (0.010)	126 (24.706)	124,711	123 (0.099)	58 (47.154)	5,345,377	633 (0.012)	184 (29.068)	407	278 (68.305)	117 (42.086)

Note: linear χ^2 test.
χ^2 test.
* $P<.01$, compared with outpatients.
† $P<.01$, compared with the previous 3 years.
‡ $P<.01$, compared with the previous 3 years.

Table 4

Comparison of the HCV RNA-positive rates of outpatients and inpatients between surgical and non-surgical departments from 2014 to 2017.

	Outpatients				Inpatients				Outpatients + Inpatients			
	Surgical departments		Nonsurgical departments		Surgical departments		Nonsurgical departments		Surgical departments		Nonsurgical departments	
Year	Detectio-n cases	Positive cases, rate (%)	Detection cases	Positive cases, rate (%)	Detection cases	Positive cases, rate (%)	Detectio-n cases	Positive cases, rate (%)	Detectio-n cases	Positive cases, rate (%)	Detection cases	Positive cases, rate (%)
2014	0	0 (N/A)	78	21 (26.923)*	0	0 (N/A)	17	8 (47.059)*	0	0 (N/A)	95	29 (30.526)*
2015	2	0 (0.000)	109	26 (23.853)*	9	6 (66.667)	20	6 (30.000)*	11	6 (54.545)	129	32 (24.806)*
2016	2	0 (0.000)	132	30 (22.727)*	7	4 (57.143)	17	7 (41.176)*	9	4 (44.444)	149	37 (24.832)*
2017	2	0 (0.000)	185	49 (26.486)*	25	11 (44.000)†	28	16 (57.143)‡,*	27	11 (40.741)§	213	65 (30.516)*
Total	6	0 (0.000)	504	126 (25.000)*	41	21 (51.220)	82	37 (45.122)*	47	21 (44.681)	586	163 (27.816)*

Note: linear χ^2 test. N/A = not available.
χ^2 test.
* $P<.01$, compared with surgical department.
† $P<.01$, compared with the previous 3 years.
‡ $P<.01$, compared with the previous 3 years.
§ $P<.01$, compared with the previous 3 years.

positive rates of anti-HCV in inpatients from nonsurgical departments were significantly higher ($P<.01$) (Table 4).

3.3. Positive rates of anti-HCV and HCV RNA and new hepatitis C cases diagnosed from different clinical departments

Both the detection numbers and positive numbers of HCV-RNA were concentrated in the nonsurgical departments such as hepatology-infection, nephrology, gastroenterology and the surgical departments of orthopedics, general surgery, and obstetrics. Among the 151 new hepatitis C cases diagnosed from 2014 to 2017, 124 cases were diagnosed by nonsurgical departments, mostly by the departments of hepatology-infection, gastroenterology, and nephrology; 27 cases were diagnosed by surgical departments, mostly by the departments of orthopedics and obstetrics. Interestingly, 81 cases were diagnosed after the project was implemented in 2017, exceeding

Table 5

The positive rates of anti-HCV and HCV RNA and new hepatitis C cases diagnosed from different clinical departments.

	Anti-HCV		HCV-RNA		New hepatitis C cases diagnosed	
Departments	Detection cases	Positive cases, rate (%)	Detection cases	Positive cases, rate (%)	Total cases	Diagnosed in 2017 (a ratio of 4 years, %)
Surgical departments						
Gynecology	22,051	26 (0.118)	5	0 (0.000)	4	4 (100.000)
Obstetrics	17,245	20 (0.116)	6	4 (66.667)	3	1 (33.333)
Orthopedics	7560	26 (0.344)	13	9 (69.231)	8	4 (50.000)
General surgery	7306	28 (0.383)	12	1 (8.333)	3	2 (66.667)
Neurosurgery	1698	3 (0.177)	1	1 (100.000)	2	0 (0.000)
Urology	7045	19 (0.270)	4	2 (50.000)	3	1 (33.333)
Colorectal and anal surgery	2586	5 (0.193)	2	1 (50.000)	1	1 (100.000)
Thoracic surgery	1102	4 (0.363)	2	2 (100.000)	2	1 (50.000)
Otolaryngology	1255	1 (0.080)	1	0 (0.000)	0	1 (100.000)
Ophthalmology	851	4 (0.470)	1	1 (100.000)	1	1 (100.000)
Stomatology	110	0 (0.000)	0	0 (N/A)	0	0 (N/A)
Pain management	45	0 (0.000)	0	0 (N/A)	0	0 (N/A)
Nonsurgical departments						
Hepatology-infections	6966	100 (1.436)	463	126 (27.214)	84	43 (51.190)
Endocrinology	754	2 (0.265)	5	2 (40.000)	4	1 (25.000)
ICU	414	2 (0.483)	1	1 (100.000)	1	0 (0.000)
Pediatrics	992	9 (0.907)	2	0 (0.000)	1	0 (0.000)
Neurology	4031	8 (0.198)	3	1 (33.333)	3	2 (66.667)
Respiratory medicine	1728	5 (0.289)	3	3 (100.000)	4	3 (75.000)
Cardiology	2125	8 (0.376)	4	0 (0.000)	1	1 (100.000)
Hematology and oncology	555	1 (0.180)	1	1 (100.000)	1	1 (100.000)
Rehabilitation medicine	11	0 (0.000)	0	0 (N/A)	0	0 (N/A)
Nephrology	3539	78 (2.204)	69	19 (27.536)	5	5 (100.000)
Gastroenterology	6607	27 (0.409)	15	7 (46.667)	17	8 (47.059)
Dermatology	588	0 (0.000)	0	0 (N/A)	0	0 (N/A)
Chinese medicine	162	1 (0.617)	0	0 (N/A)	0	0 (N/A)
Emergency medicine	4923	22 (0.447)	6	1 (16.667)	**3**	2 (66.667)
Psychology	18	0 (0.000)	0	0 (N/A)	0	0 (N/A)
General medicine	661	8 (1.210)	14	2 (14.286)	0	0 (N/A)
SUM	102,928	407 (0.395)	633	184 (29.068)	151	81 (53.642)

N/A = not available.

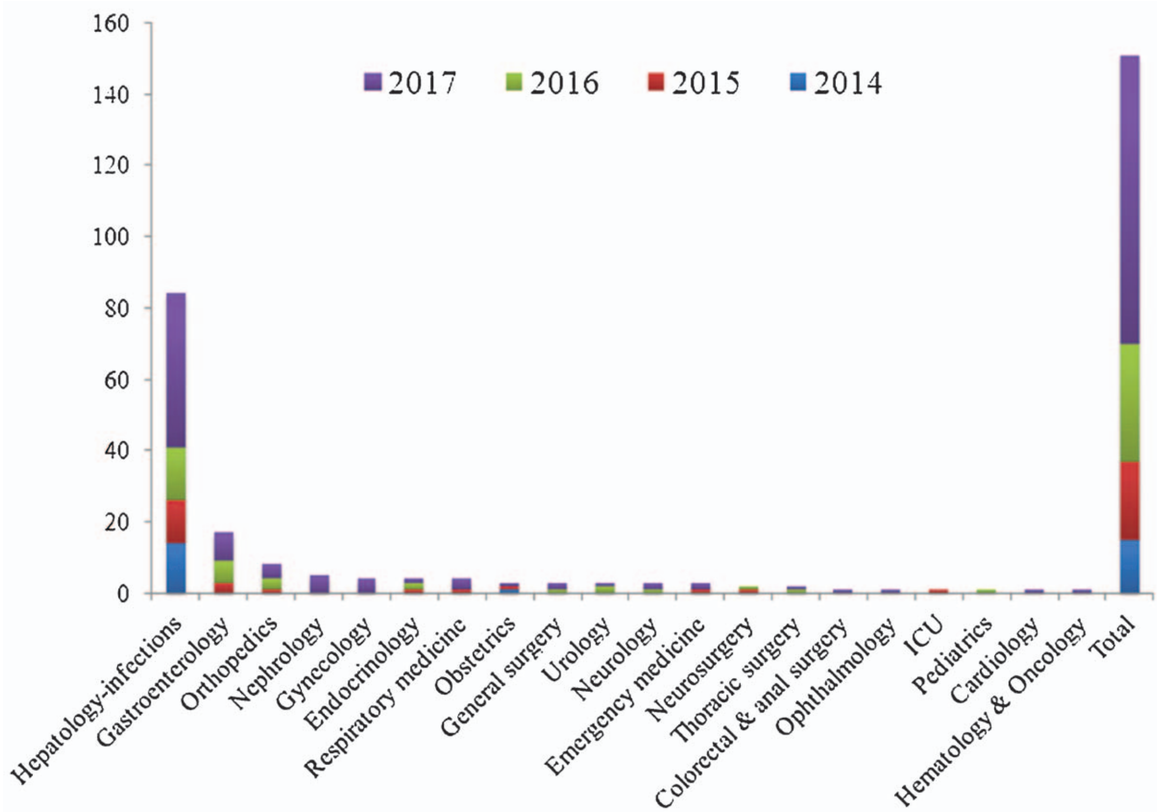

Figure 2. The comparisons of the new hepatitis C virus cases diagnosed among different clinical departments from 2014 to 2017.

the total number of 70 cases over the previous 3 years (Table 5, Fig. 2).

4. Discussion

In 2016, WHO proposed a global public health goal to eliminate hepatitis C hazards by 2030, referred to as the "2030 Target." HCV infection control is essential for preventing the development of decompensated cirrhosis and hepatology cancer caused by hepatitis C. However, most cases of post-hepatitis hepatology cancer have significantly impeded this goal because of lack of clinical manifestations.[15,16] A method to find HCV infection as early as possible, such as expanding the populations included in HCV screening, is considered a useful preventive strategy to discover undiagnosed hepatitis C patients at an early stage and reduce the occurrence of hepatology cirrhosis.[7] Therefore, China's CDC STD/AIDS Prevention and Control Center initiated a pilot research project of hospital-based hepatitis C epidemic surveillance in 2017 for exploring the effectiveness of expanding the target populations of HCV screening in hospitals.[17]

Before this pilot research, the overall positive rate of anti-HCV in all patients in Beilun Branch of the First Affiliated Hospital, College of Medicine, Zhejiang University was 0.395%, which is close to the positive rate of anti-HCV in residents of the eastern region of China reported in 2006 (0.37%).[11] However, after expanding the anti-HCV detection to include the high-risk population of hepatitis C infections, more positive cases of anti-HCV (0.533%) were found indicating that the infection prevalence of HCV reported in 2006 might not reflect the actual HCV infection situation in China. Although false positive of anti-HCV may exist, the increase of the positive rate of anti-HCV in 2017 could not be fully attributed to this reason. After the implementation of the pilot, with the increase of detection rate of HCV RNA in antibody-positive patients, the positive cases of HCV RNA were significantly enhanced than before, indicating that more active HCV infection patients with no clinical manifestations could be found by this expanding anti-HCV screening. At the same time, this result also suggests that efforts to expand anti-HCV detection should focus more on the high-risk population rather than on the general population.

In this study, the overall positive rate (42.086%) of HCV-RNA in the positive patients of anti-HCV is much higher than that (18.9%) in the general population of Wuhan reported by Niu et al in 2016.[18] First, compared with the general population, HCV-RNA-positive cases might be easier to identify through various laboratory tests performed in the hospital for positive patients of anti-HCV.[19] Second, before implementation of this project, it was the physicians' decision to check the HCV-RNA in anti-HCV-positive patients with normal or abnormal liver function. After implementation of this project, all anti-HCV-positive patients were asked to test HCV-RNA regardless of the patient's liver function. As a result, the detection rate of HCV-RNA in anti-HCV-positive patients significantly increased from 58.333% in 2014 to 88.820% in 2017. Through this expanding HCV-RNA detection strategy, the positive cases of HCV-RNA with normal liver function were also found. As a result, the positive rate of HCV-RNA in the anti-HCV-positive patients increased from 35.714% in 2014 to 45.455% in 2017. However, it is worth noting that less than half of anti-HCV-positive patients were found to be HCV-RNA-positive in this study. The reason for such a low HCV-RNA-positive rate may not all attributed to false-positive in anti-HCV as mentioned above; another possible reason may attribute to the less sensitivity of our laboratory HCV RNA detecting methods. In addition, our results also indicate that choosing high-risk HCV patients in hospital as the target population is a useful strategy for detecting HCV infection cases.

The inpatients received HCV detection as a routine test especially for the inpatients of meeting screening criteria. However, the outpatients received a hepatitis C-related detection only if clinical manifestations or abnormal liver function occurred, so it is not surprising that the detection rate of anti-HCV in the outpatients (0.588%) was much lower than that in the inpatients (57.928%). The positive rate of anti-HCV in the outpatients (0.688%) was much higher than in the inpatients (0.271%), which may be explained by the fact that only select populations were checked in the outpatients. Further analysis showed that the positive rate of HCV-RNA in the outpatients (24.706%) was significantly lower than that in the inpatients (47.154%). This phenomenon may be caused by heavier hepatic damage in the inpatients than in the outpatients. Our results also suggest that the outpatient department, which has contact with the most patients, can find more patients with HCV by expanding anti-HCV tests; however, the inpatient ward can be used as an important place to confirm HCV infection.

The overall positive numbers of anti-HCV and HCV-RNA of nonsurgical departments were higher than those of surgical departments, especially in hepatology-infection, nephrology, and gastroenterology. This is because the patients with abnormal liver function or HCV infection were always directed to hepatology-infection or gastroenterology departments. And hemodialysis patients of the nephrology department were advised to check anti-HCV quarterly as a routine.[20,21] But, through the pilot research, the positive numbers of anti-HCV and HCV-RNA of the surgical departments were significantly increased due to the needs of preoperative examinations for inpatients and the requirements of expanding the screening of HCV, especially in the departments of obstetrics and orthopedics because these 2 departments received the most cases in our hospital. So, although most cases (124/151) were diagnosed by nonsurgical departments, the upward trend of the proportion of cases diagnosed by surgical departments should not be ignored. Meanwhile, the positive rates of HCV-RNA in the inpatients of the surgical departments were higher compared to the inpatients of the nonsurgical departments. Therefore, surgical departments should pay more attention to the detection of HCV-RNA in inpatients to easily find confirmed cases by expanded screening of HCV-RNA.[22,23]

5. Conclusion

Through the pilot research on hospital-based hepatitis C epidemic surveillance, 81 cases were diagnosed after implementation of this project in 2017, exceeding the total number of the previous 3 years. This study suggests that expanding the screening of anti-HCV and HCV-RNA in the target populations can lead to detection of more HCV cases, including patients with normal liver function.[19,24,25] Moreover, this study was conducted as part of a Hepatitis C sero-epidemiology of clinical patients in hospitals, which will provide valuable evidence-based information for public health research, policy, and preventive programming priorities at the national and regional levels.[26–33]

This study was limited by the following factors: many HCV occult patients were diagnosed through the pilot research, but it was not clear how many actual cases were still missed; the differences of anti-HCV and HCV-RNA tests among the departments may be due to detection bias, which was derived from the patients' condition as well as the doctors' willingness; the effectiveness of this pilot research had no parallel comparison with other research projects.

Acknowledgments

The authors thank Ms. Jenny Bowman for her assistance in the preparation of this article. The support and cooperation from all medical departments of our hospital were also very important to fulfilling this study.

Author contributions

Conceptualization: Dongxian Ye, Chunxia Xu, Jinshun Zhao.
Data curation: Dongxian Ye, Yuanliang Gu, Libo Zhang, Youping Zhang, Chunxia Xu.
Formal analysis: Dongxian Ye, Yuanliang Gu, Libo Zhang, Youping Zhang.
Investigation: Dongxian Ye, Yuanliang Gu, Libo Zhang.
Methodology: Dongxian Ye, Yuqing Tang, Yuanliang Gu, Libo Zhang.
Project administration: Dongxian Ye, Youping Zhang, Chunxia Xu .
Resources: Youping Zhang, Chunxia Xu .
Software: Dongxian Ye, Yuqing Tang, Harris Haleem.
Supervision: Dongxian Ye.
Validation: Dongxian Ye, Yuanliang Gu, Libo Zhang.
Visualization: Yuanliang Gu, Dongxian Ye, Yuqing Tang.
Writing – original draft: Dongxian Ye, Yuqing Tang, Chunxia Xu.
Writing – review & editing: Dongxian Ye, Yuqing Tang, Chunxia Xu, Jinshun Zhao.

References

[1] Denniston MM, Jiles RB, Drobeniuc J, et al. Chronic hepatitis C virus infection in the United States, National Health and Nutrition Examination Survey 2003 to 2010. Ann Intern Med 2014;160:293–300.
[2] Lingala S, Ghany MG. Natural history of hepatitis C. Gastroenterol Clin North Am 2015;44:717–34.
[3] Petruzziello A, Marigliano S, Loquercio G, et al. Global epidemiology of hepatitis C virus infection: an up-date of the distribution and circulation of hepatitis C virus genotypes. World J Gastroenterol 2016;22:7824–40.
[4] Sanlidag T, Akcali S, Ecemis T, et al. [Investigation of the correlation between anti-HCV levels (S/Co) with HCV-RNA in the diagnosis of hepatitis C virus (HCV) infection]. Mikrobiyol Bul 2016;50:508–10.
[5] Wang D, Le XH, Luque AE. Identifying effective approaches for dissemination of clinical evidence—correlation analyses on promotional activities and usage of a guideline-driven interactive case simulation tool in a statewide HIV-HCV-STD Clinical Education Program. Stud Health Technol Inform 2015;216:515–9.
[6] Holmes JA, Chung RT. Viral hepatitis: HCV compartmentalization in HCC: driver, passenger or both? Nat Rev Gastroenterol Hepatol 2016;13:254–6.
[7] Coffin PO, Reynolds A. Ending hepatitis C in the United States: the role of screening. Hepat Med 2014;6:79–87.
[8] Mohd Hanafiah K, Groeger J, Flaxman AD, et al. Global epidemiology of hepatitis C virus infection: new estimates of age-specific antibody to HCV seroprevalence. Hepatology 2013;57:1333–42.
[9] Hajarizadeh B, Grebely J, Dore GJ. Epidemiology and natural history of HCV infection. Nat Rev Gastroenterol Hepatol 2013;10:553–62.

[10] Zhicheng D, Guoming Y. Viral Hepatitis In China: Seroepidemiological Study of Chinese Population 1992–1995 (Part One). 1997;Science and Technology Press,

[11] Chen YS, Li L, Cui FQ, et al. A sero-epidemiological study on hepatitis C in China. Chin J Epidemiol 2011;32:888–91.

[12] Tanaka M, Katayama F, Kato H, et al. Hepatitis B and C virus infection and hepatocellular carcinoma in China: a review of epidemiology and control measures. J Epidemiol 2011;21:401–16.

[13] Prakash S, Shukla S, Ramakrishna V, et al. Distribution of hepatitis C genotypes in Uttar Pradesh, India; rare genotype 4 detected. J Med Virol 2018;90:1875–81.

[14] Xu AQ, Zhang L. The review and significance of national seroepidemiological surveys on viral hepatitis in China. Chin J Pre 2017;51:457–61.

[15] Hajarizadeh B, Grebely J, Dore GJ. Case definitions for acute hepatitis C virus infection: a systematic review. J Hepatol 2012;57:1349–60.

[16] Liang TJ, Rehermann B, Seeff LB, et al. Pathogenesis, natural history, treatment, and prevention of hepatitis C. Ann Intern Med 2000; 132:296–305.

[17] Al-Busafi SA, Al-Shuaili H, Omar H, et al. Epidemiology of chronic hepatitis C infections at a tertiary care centre in Oman. Sultan Qaboos Univ Med J 2017;17:e404–10.

[18] Niu Z, Zhang P, Tong Y. Age and gender distribution of Hepatitis C virus prevalence and genotypes of individuals of physical examination in WuHan, Central China. Springerplus 2016;5:1557.

[19] Mahmud S, Akbarzadeh V, Abu-Raddad LJ. The epidemiology of hepatitis C virus in Iran: Systematic review and meta-analyses. Sci Rep 2018;8:150.

[20] Abdo AA, Sanai FM, Al-Faleh FZ. Epidemiology of viral hepatitis in Saudi Arabia: are we off the hook? Saudi J Gastroenterol 2012;18:349–57.

[21] Di Costanzo GG, De Luca M, Tritto G, et al. Effect of alcohol, cigarette smoking, and diabetes on occurrence of hepatocellular carcinoma in patients with transfusion-acquired hepatitis C virus infection who develop cirrhosis. Eur J Gastroenterol Hepatol 2008;20:674–9.

[22] Konerman MA, Yapali S, Lok AS. Systematic review: identifying patients with chronic hepatitis C in need of early treatment and intensive monitoring–predictors and predictive models of disease progression. Aliment Pharmacol Ther 2014;40:863–79.

[23] Perz JF, Grytdal S, Beck S, et al. Case-control study of hepatitis B and hepatitis C in older adults: do healthcare exposures contribute to burden of new infections? Hepatology 2013;57:917–24.

[24] Taherkhani R, Farshadpour F. Global elimination of hepatitis C virus infection: progresses and the remaining challenges. World J Hepatol 2017;9:1239–52.

[25] Yin Z, Zhangpin L. Clinical significance of anti-HCV and HCV-RNA detectionfor hepatitis C patients. Journal of Yanan University 2017; 15:58–60.

[26] Ayoub HH, Abu-Raddad LJ. Impact of treatment on hepatitis C virus transmission and incidence in Egypt: a case for treatment as prevention. J Viral Hepat 2017;24:486–95.

[27] Chaabna K, Kouyoumjian SP, Abu-Raddad LJ. Hepatitis C virus epidemiology in Djibouti, Somalia, Sudan, and Yemen: systematic review and meta-analysis. PLoS One 2016;11:e0149966.

[28] Chaabna K, Mohamoud YA, Chemaitelly H, et al. Protocol for a systematic review and meta-analysis of hepatitis C virus (HCV) prevalence and incidence in the Horn of Africa sub-region of the Middle East and North Africa. Syst Rev 2014;3:146.

[29] Ashkani-Esfahani S, Alavian SM, Salehi-Marzijarani M. Prevalence of hepatitis C virus infection among hemodialysis patients in the Middle-East: a systematic review and meta-analysis. World J Gastroenterol 2017;23:151–66.

[30] Fadlalla FA, Mohamoud YA, Mumtaz GR, et al. The epidemiology of hepatitis C virus in the Maghreb region: systematic review and meta-analyses. PLoS One 2015;10:e0121873.

[31] Heijnen M, Mumtaz GR, Abu-Raddad LJ. Status of HIV and hepatitis C virus infections among prisoners in the Middle East and North Africa: review and synthesis. J Int AIDS Soc 2016;19:20873.

[32] Mahmud S, Al-Kanaani Z, Chemaitelly H, et al. Hepatitis C virus genotypes in the Middle East and North Africa: distribution, diversity, and patterns. J Med Virol 2018;90:131–41.

[33] Mohamoud YA, Mumtaz GR, Riome S, et al. The epidemiology of hepatitis C virus in Egypt: a systematic review and data synthesis. BMC Infect Dis 2013;13:288.