

Shift in New HIV/AIDS Epidemic and Factors Associated with False Positives for HIV Testing: A Retrospective Study from 2013 to 2018 in Xi'an, China

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Research article

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Abstract

Objectives: In the study, firstly, the epidemic characteristics of new HIV/AIDS were investigated in order to provide evidence for the targeted interventions; Secondly, the major factors of false positives (FP) for HIV testing were also determined. **Methods:** A retrospective review was performed in a teaching hospital in Xi'an between 2013 and 2018. The overall characteristics and epidemiological trends of new HIV/AIDS were described. Moreover, the distributions of FP cases in the gender, age and department were analysed, and the major factors of FP were determined by the Pareto analysis. **Results:** During the study, a total of 469 new HIV/AIDS were diagnosed, with an increasing prevalence from 0.0626% in 2013 to 0.0827% in 2018. Of them, the majority occurred in the Hans (99.57%), males (88.50%), people aged 21-50 years (76.97%), migrants (60.98%) and sexual contact route (88.70%). A rapid increase in the annual number of new HIV/AIDS and multiple routes of HIV transmission were found. The epidemic showed increasing trends in groups of young individuals, students and homosexual mode, however, a downward trend in the percentage of injecting drug use was also observed. 67.81% of FP cases were over 50 years old. The departments of oncology, obstetrics, hepatobiliary surgery, nephrology, cardiology and infectious disease were major factors of FP by Pareto analysis. **Conclusions:** The HIV/AIDS epidemic in Xi'an is still evolving, therefore, effective strategies, appropriate education and scaling up HIV testing should be developed to control the spread of the epidemic. In addition, old adults and specific departments were associated with FP.

Background

Since the first AIDS case was identified in 1985 in Beijing, the HIV/AIDS epidemic had reached all 31 provinces/autonomous regions/municipalities in China in 1998.¹⁻³ In China, the national prevalence is still low (less than 0.1%),^{4,5} however, the epidemic varies geographically, and the newly HIV infections and AIDS cases increase annually.⁶⁻⁸ By the end of September 2018, there were 849,602 people living with HIV (PLWH) in mainland China.⁹ The epidemic is severe in some midwest provinces (Sichuan, Chongqing, Guizhou, Hunan, Henan) and border communities (Xinjiang, Guangxi, Guangdong), with annual new HIV/AIDS cases more than 5000.¹⁰

The first HIV infection was reported in Shaanxi in 1994.¹¹ From then on, acceleration in the incidence of HIV/AIDS is evident. Comparing with 2004, Shaanxi had the top three highest relative increase in the incidence of HIV infection (Relative change: 1.40) and high relative increase in the incidence of AIDS (Relative change: 1.43) in China in 2014.¹² The annual new HIV/AIDS cases were more than 1000 since 2015.¹³ Up to present, the resident population of Xi'an city is more than 10 millions and accounts for nearly one third of the total population of Shaanxi Province. The study was from patients in the First Affiliated Hospital of Xi'an Jiaotong University, which is the largest hospital in Northwest China and has the top two largest numbers of diagnosed HIV/AIDS cases every year in Xi'an. Thus, the study can be useful to BETTER UNDERSTAND THE demographic constitution of HIV in Xi'an city and Shaanxi Province, MOREOVER, the factors of false positives (FP) FOR HIV SCREENING WERE ALSO ANALYZED.

Methods

Study population

This study was conducted between January 1, 2013 and October 31, 2018. All data were captured from the LIS and HIS of the First Affiliated Hospital of Xi'an Jiaotong University, and Xi'an, Center for Disease Control and Prevention (CDC), Shaanxi Province, China. During the study period, 622,164 patients underwent HIV screening, and 25 subjects previously confirmed as HIV/AIDS were excluded. Thus, a total of 622,139 cases were included in the study.

HIV routine test

A 4th-generation kit, Architect HIV Ag/Ab Combo (Abbott Diagnostics, Abbott Park, IL) and a 3rd-generation EIA kit, XinChuang HIV-1/2Ab (InTec, INC, XiaMen, FuJian, China) were used as routine test for HIV. COI or S/CO ≥ 1 was defined as reactive, and COI or S/CO < 1 was defined as non-reactive.

Western blotting

Western blotting HIV1/2 BLOT 2.2 (MP Biomedicals, Singapore) is conducted and interpreted by the Xi'an CDC. Positive (HIV-1)—The presence of at least two bands, including two *env* bands or one *env* band and one p24 band (.before 2017); The presence of at least two *env* bands and one *gag* or one *pol* band (since 2017); Positive (HIV-2)—The presence of gp36 band indicates HIV-2 infection. Indeterminate—reactivity to any of the bands but not compatible with the criteria for a positive interpretation; Negative—the absence of any of the specific bands.

Statistical analysis

Statistical analyses were conducted by SPSS13.0 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics were used for the demographic constitution. Variables for false positives (FP) were evaluated by Pareto analysis, and those which were in the cumulative constituent ratios of 0-80%, 80-90% and 90-100%, should be defined as Main (class A), Secondary (class B) and General factors (class C) for FP, respectively.

Results

Overall characteristics of HIV testing

During the study period, a total of 622,139 subjects were included, with a male/female ratio of 1.003 and a median age of 50 years (Rang: 9 days to 96 years). Among them, 469 new HIV/AIDS cases were

diagnosed. With a sharp growth in the testing subjects, the number of newly diagnosed cases and prevalence rate for HIV/AIDS have shown an increasing trend every year. Since 2015, the 4th-generation assay has been the predominant method for HIV screening, which resulted in a drastic increasing in the false-positive ratio (FPR). In addition, among the reactive cases for HIV screening, the not-diagnosed ratio (NDR) of the subjects who were lost to follow-up or less than 18 months age remained relatively stable (Rang: 9.09% to 15.0%), Table 1& Fig 1.

Features of false positives (FP)

Of the 292 false positives from 2013 to 2018, 55.82% were male and 44.18% were female with a median age of 51 years (range: 16-86 years). In terms of age-specific distribution, 11.3%, 10.96%, 9.83% and 67.81% were at 30, 31-40, 41-50 and 51 years old, respectively. The Pareto analysis showed that 5.14%-27.74% were from the department of oncology, obstetrics, hepatobiliary surgery, nephrology, cardiology, infectious disease and rheumatology with a cumulative ratio of 83.56%, which can be categorized as class A (major factors) associated with FP, Table 2& Fig 2.

The demographic constitution of new HIV/AIDS and shift in epidemic

Of the new HIV/AIDS cases, most were Hans (99.57%), males (88.50%), people aged 21-50 years (76.97%), migrants (60.98%) and sexual contact route (88.70%), with a male/female ratio of 5.9:1 and a median age of 39 years (range: 2-76 years). In terms of marital status, 59.49%, 35.61% and 4.9% were married, unmarried and widowed/divorced, respectively. The constitutions of students, unemployed/informal employees, formal employees, peasants and retiree were 13.43%, 43.92%, 18.55%, 9.13% and 9.38%, respectively. 63.75%, 24.95%, 4.9%, 0.64%, 0.21% and 5.35% of the cases were infected through heterosexual contact, homosexual contact, injecting drug use (IDU), mother to child, blood and unknown, respectively. The new HIV/AIDS cases spread across Shaanxi province, of them, 38.98%, 44.77% and 16.26% were from Xi'an, other areas in Shaanxi and other provinces, Table 3. Among the 175 cases in Xi'an, 73.14% were from Changan(n=65), Yanta(n=40) and Beilin(n=29) districts, Fig 3A. In addition, Xianyang(n=54), Weinan(n=52) and Ankang(n=28) cities consisted of 66.67% of the cases(n=201) in other areas in Shaanxi province, Fig 3B. Gansu(n=21), Henan(n=20) and Shanxi(n=12) were the top three prefectures that had the largest numbers of cases in other provinces.

Over the six years, the epidemic of new HIV/AIDS had showed an increasing trend in the individuals who were <20 years age (from 2.44% in 2013 to 6.09% in 2018), 21-30 years age (from 24.39% in 2013 to 31.3%), students (from 7.32% in 2013 to 15.46% in 2018) and homosexual mode (from 19.51% in 2013 to 26.96% in 2018), however, the percentage of injecting drug use had decreased from 7.32% in 2013 to 4.35% in 2018. In addition, the epidemic in sex, other groups for age, job and transmission mode had remained relatively stable, Fig 4.

Discussion

The research data was from 622,139 subjects in Xi'an, and the MAIN FINDINGS OF THIS STUDY WERE: (1) The new HIV/AIDS cases and constituent ratios of students and young people increased yearly, however, the HIV prevalence remained still low; (2) Most of the HIV infections occurred in the Hans, males, young and middle-aged populations and migrants; meanwhile, the HIV/AIDS epidemic had spread across Shaanxi. The local infections were concentrated in Changan, Yanta and Beilin districts, however, most the infections of other areas in Shaanxi province were from Xianyang, Weinan and Ankang cities; (3) Multiple routes of HIV transmission were co-existent, in which the sexual contact was predominant and IDU route had decreased, however, the blood and vertical transmission were rarely observed; (4) The old adults and specific departments, i.e., oncology, obstetrics, hepatobiliary surgery, nephrology, cardiology and infectious disease, were associated with FP.

Xi'an is not only a famous tourist city, but also an important central city in Western China. In addition, more than 30 universities with nearly a million students are located here. The large numbers of migrant workers, tourists, students play a "bridge" for the HIV/AIDS transmitting.¹⁴ With the implementation of testing-based prevention for infectious diseases (HIV, HBV, HCV and Syphilis) for pregnant women,¹⁵ before operation, interventional examination or treatment, the testing and confirmed cases for HIV increase yearly in China.^{12,16} In addition, substantial intervention initiatives, such as "Four Free One Care"¹⁷ and "prevention of mother-to-child transmission (PMTCT) programme",¹⁸ have been introduced since 2003. which result in an obvious decrease in the proportion of HIV cases attributed to vertical transmission in China.¹⁹ A rapid increase in the testing number and low constituent ratio of mother-to-child transmission for HIV/AIDS were also observed in the study.

China's HIV/AIDS epidemic began in the 1990s among injecting heroin users and commercial plasma donors.²⁰ Quite a few control policies, i.e., "law against drug use",²¹ "voluntary and compulsory detoxification",²² "methadone maintenance treatment (MMT) program",²³ and "commercial blood/plasma collection stations shut down and blood donors must be tested for HIV since 1995",²⁴ HAVE BEEN MADE AND PERFORMED EFFECTIVELY IN CHINA, which lead to the ratios of both IDU and blood routes among new infections decrease yearly.^{5,25} Simultaneously, there is a remarkable rise in both commercial sexual work at entertainment and extramarital sex via social apps in recent years. Thus, unsafe sexual behaviors have been the major cause of HIV infection in China.²⁶ In the study, the sexual contact was the most prominent route of HIV transmission in Xi'an, accounting for 88.6% of the cases, which was similar to other studies in China.³⁻⁵

Recently, it is notable that the HIV/AIDS epidemic in adolescents/students and older adults is significant increase in China.^{3,5,27} However, they are not usually considered as the high-risk population and are less likely to be tested for HIV. During the study period, the proportion of students among HIV cases increased yearly. In addition, the constituent ratios of HIV cases that were attributed to the students, -20 and 51-

years age groups were 13.36%, 6.24% and 16.7%, respectively. Therefore, scaling up HIV prevention education and testing should be covered in both the high-risk population and the general population.

Another emerging theme in China is that a large number of PLWH are unaware of their infection status.^{28,29} Owing to be in poor economic condition, fear of privacy being leaked and being STIGMATIZED, many high-risk people do not visit the hospital for HIV testing, which results in a high percentage of PLWH that can not be diagnosed. In the study, heterosexuality was the dominant transmission route (63.92%), however, the proportion of HIV cases attributed to female was only 14.48%. Meanwhile, the not-diagnosed ratio of the reactive cases for screening test fluctuated between 9.09% and 14.92%.

In China, people are sensitive to the HIV/AIDS topics, thus, more attention should also be paid to false positives (FP) for HIV screening test. In the study, 47.69% of FP cases were over 60 years of age. By department distribution, the oncology, obstetrics, hepatobiliary surgery, nephrology, cardiology, infectious disease and rheumatology were major factors associated with FP, with a cumulative ratio of 83.56%.

Conclusions

In Xi'an city, the HIV/AIDS prevalence is still low, and dramatic reductions in the HIV infections via IDU, blood and vertical transmission have also been achieved. However, the annual number of new HIV infections has increased rapidly. The targeted interventions for HIV/AIDS epidemic in Xi'an should be implemented as followings: First, the awareness of transmission routes, prevention for HIV infection should be strengthened further among the public to increase the using of condoms; Second, the HIV epidemic in migrants, adolescents/students and older individuals should be more concerned, and scaling up HIV testing should be covered in both the high-risk population and the general population to improve the diagnostic rate of HIV infection and reduce the risk for further transmission.

Declarations

Acknowledgments

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AVAILABILITY OF DATA AND MATERIAL

The data used in the study was available from Xi'an CDC and LIS of the First Affiliated Hospital of Xi'an Jiaotong University.

Authors' contributions

LW and JYW were major contributors in the writing of the manuscript. LW, KGZ and WC were responsible for the study design. The statistical analysis and figure of the study were performed by JYW, KGZ, JXR, WC and LW .

Ethics Statement

The study was deemed exempt from review by the Ethics Committee of the First Affiliated Hospital of Xi'an Jiaotong University as routine data for clinical purposes were used, and all patient information remained confidential in the study.

CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

JYW, KGZ, JXR, WC and LW have read and approved the final manuscript for publication in BMC Infectious Diseases.

COMPETING INTERESTS

JYW, KGZ, JXR, WC and LW declare no financial or other conflict of interest.

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Tables

Table 1: Overall characteristics of HIV testing from 2013 to 2018.

Years	Testing cases				Reactive cases				Overall			
	Male	Female	Using 3rd-generation	Using 4th-generation	Total	New HIV/AIDS	FP	ND	Total	Prevalence (/10000)	FPR (%)	NDR (%)
2013	32666	32837	60320	5183	65503	41	9	5	55	6.26	18.00	9.09
2014	36095	36755	66663	6187	72850	53	15	9	77	7.28	22.06	11.69
2015	50009	50442	15682	84769	100451	74	62	21	157	7.37	45.59	13.38
2016	58582	59424	12235	105771	118006	89	64	27	180	7.54	41.83	15.00
2017	63358	62925	12025	114258	126283	97	66	28	191	7.68	40.49	14.66
2018	70849	68197	11652	127394	139046	115	76	25	216	8.27	39.79	11.57

Note: false-positive ratio (FPR), not-diagnosed ratio (NDR).

Table 2: Distributions of the false positives

Variables	N	%
Sex		
Male	163	55.82
Female	129	44.18
Age, years (Median: 51)		
-30	33	11.30
31-40	32	10.96
41-50	29	9.93
51-	198	67.81
Department		
Oncology	81	27.74
Obstetrics	38	13.01
Hepatobiliary Surgery	32	10.96
Nephrology	29	9.93
Cardiology	25	8.56
Infectious Disease	24	7.19
Rheumatology	15	5.14
Neurology	9	3.08
Endocrinology	8	2.74
Respiratory	7	2.40
Hematology	6	2.05
Gynaecology	5	1.71
Others	13	4.45

Table 3: The demographic constitution of new HIV/AIDS

Variables	N	%
Sex		
Male	401	85.50
Female	68	14.50
Age, years (Median: 39)		
-20	29	6.18
21-30	150	31.98
31-40	123	26.23
41-50	88	18.76
51-	79	16.84
Ethnicity		
Han	467	99.57
Minority	2	0.43
Residence		
Local area	183	39.02
Other areas in this province	210	44.78
Other provinces	76	16.20
Marital status		
Unmarried	167	35.61
Married	279	59.49
Widowed/divorced	23	4.90
Job		
Student	63	13.43
Unemployed/Informal employees	206	43.92
Formal employees	87	18.55
Peasants	44	9.38
Retiree	31	6.61
Unknown/others	38	8.10
Transmission modes		
Heterosexual	299	63.75
Homosexual	117	24.95
Injecting drug use	23	4.90
Mother to child	3	0.64
Blood	1	0.21
Unknown	26	5.54

Figures

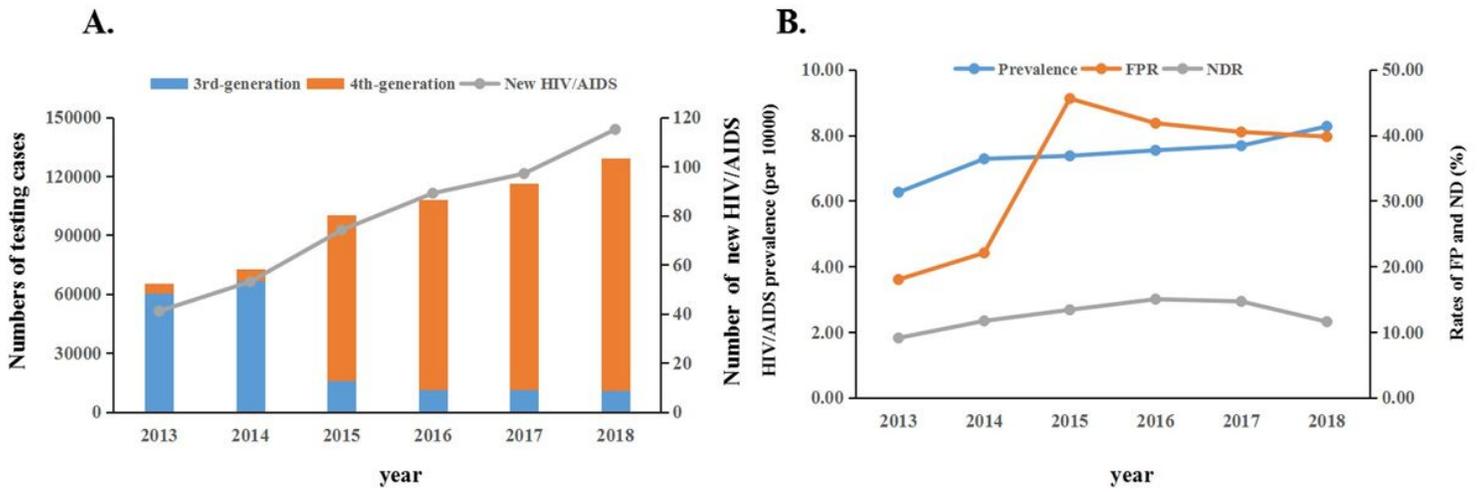


Figure 1

Overall characteristics of HIV testing, (A) the number distributions of different screening tests and new HIV/AIDS cases from 2013 to 2018; (B) the shifts in HIV prevalence, false-positive ratio (FPR) and not-diagnosed ratio (NDR) from 2013 to 2018.

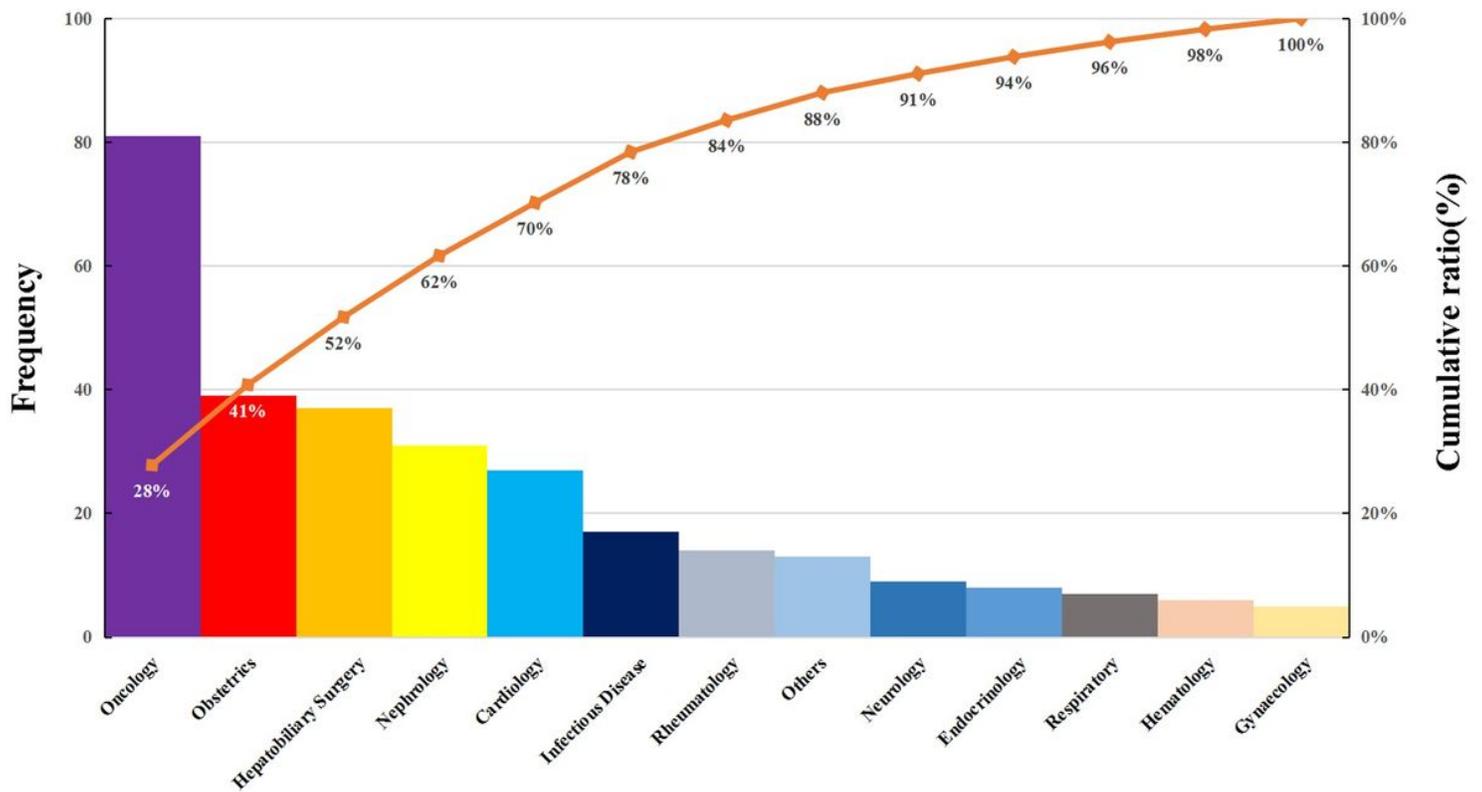


Figure 2

The department distributions of the false-positive cases

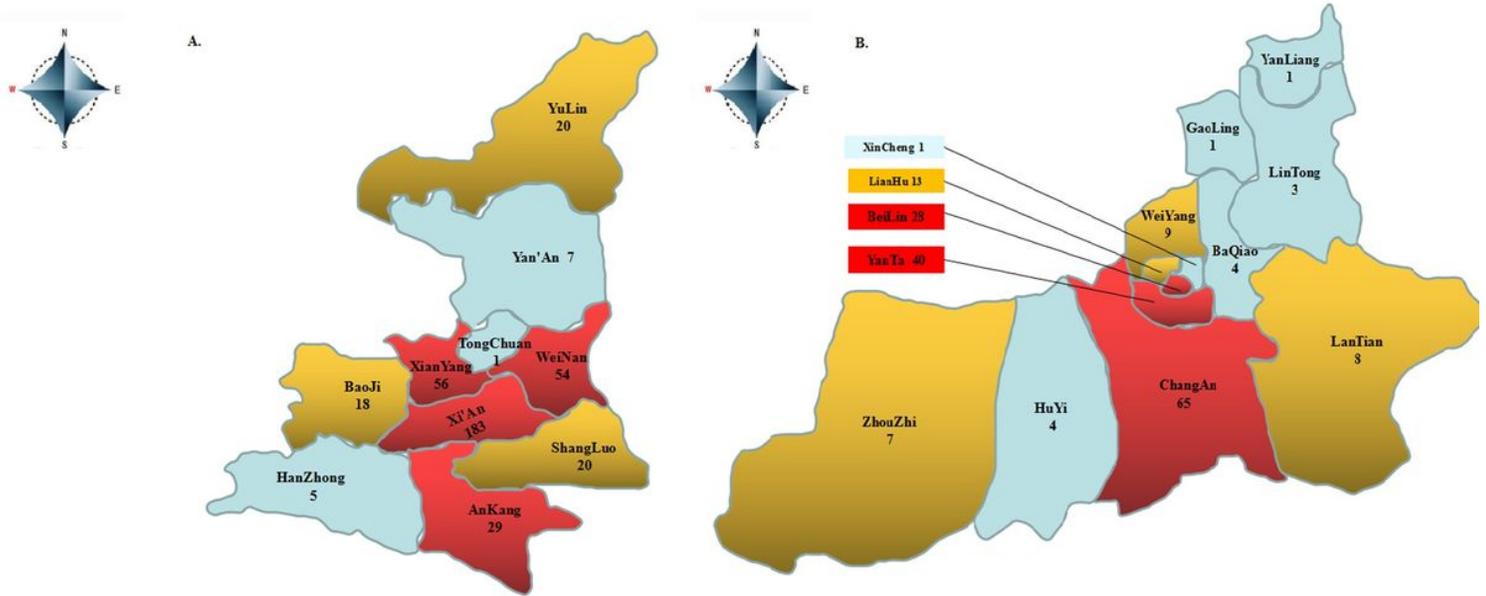


Figure 3

Geographic distribution of the new HIV/AIDS cases in (A) Xi'an city and (B) Shaanxi province.

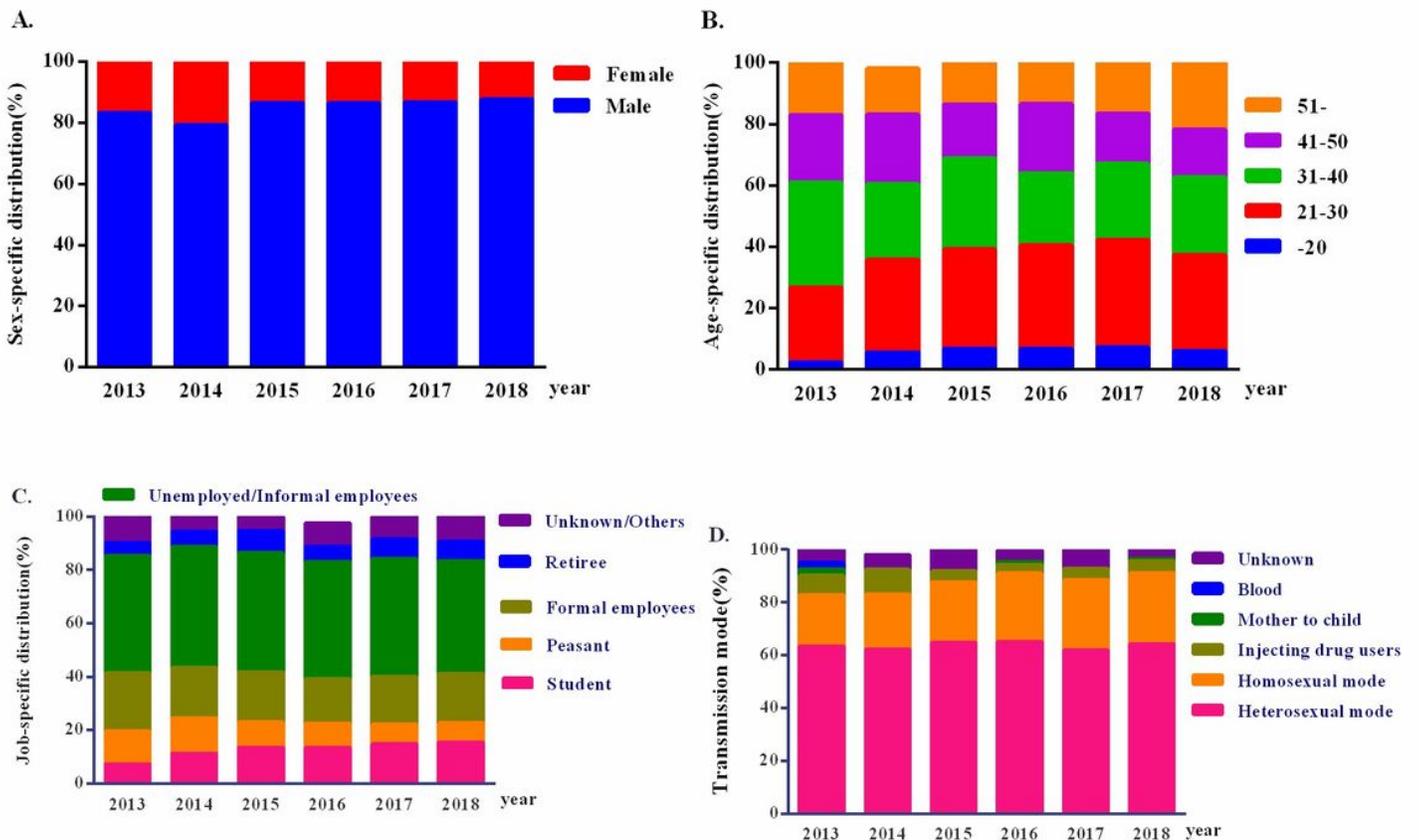


Figure 4

Distributions of the new HIV/AIDS cases from 2013 to 2018 in terms of (A) Sex; (B) Age; (C) Job and (D) Transmission mode.