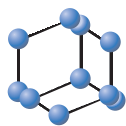


RESEARCH ARTICLE

BENTHAM
SCIENCE

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



Jing-Yuan Wang¹, Kai-Ge Zhang^{1,#}, Jing-xiong Ruan¹, Wei Chen¹ and Linchuan Wang^{1,*}

¹The First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi Province, China

Abstract: Background: In China, although quite a few bold programmes have been made for HIV/AIDS, the epidemic has still shown an increasing trend.

Objectives: The study was aimed to investigate the characteristics of new HIV/AIDS and the major factors of false positives (FP) for HIV testing.

Methods: A retrospective review was performed in a teaching hospital in Xi'an between 2013 and 2018. The overall characteristics and trends of new HIV/AIDS were described. Moreover, the major factors of FP were determined by the Pareto analysis.

Results: A total of 469 new HIV/AIDS were diagnosed, with an increasing prevalence of the new HIV/AIDS from 0.0626% (41/65503) in 2013 to 0.0827% (115/139046) in 2018. Of them, the majority occurred in the males (88.50%), people aged 21-50 years (76.97%), migrants (60.98%), and sexual contact route (88.70%). There was a rapid increase in the annual number of new HIV/AIDS and 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. Over 50 years old and patients from oncology, obstetrics, hepatobiliary surgery, nephrology, cardiology, and infectious disease constituted the major factors of FP.

Conclusion: The HIV/AIDS epidemic in Xi'an is still evolving, therefore, effective strategies, appropriate education and scaling up HIV testing should be developed. In addition, old adults and specific departments were associated with FP.

ARTICLE HISTORY

Received: October 31, 2019
Revised: March 16, 2020
Accepted: March 28, 2020

DOI:
10.2174/1570162X18666200415123607



CrossMark

Keywords: HIV/AIDS, epidemic, trends, false positives, factors, Pareto analysis.

1. INTRODUCTION

HIV infection is a serious public health issue [1-3]. 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 [4-8]. In China, the national prevalence is still low (less than 0.1%) [9-11]; however, the epidemic varies geographically, and the new HIV infections and AIDS cases increase annually [12-14]. By the end of September 2018, there were 849,602 people living with HIV (PLWH) in mainland China [15]. 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 [16-18].

The first HIV infection reported in Shaanxi was in 1994 [19]. From then on, acceleration in the incidence of HIV/AIDS is evident. Comparing with 2004, Shaanxi was

among the top three highest relative increase in the incidence of HIV infection (Relative change: 1.40) and had a high relative increase in the incidence of AIDS (Relative change: 1.43) in China in 2014 [20]. The annual new HIV/AIDS cases were more than 1000 since 2015 [21]. Up to the present, the resident population of Xi'an city is more than 10 million 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.

2. MATERIALS AND METHODS

2.1. 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

*Address correspondence to this author at the Department of Clinical Laboratory, the First Affiliated Hospital of Xi'an Jiaotong University, Xi'an, Shaanxi, China; Tel: +86-29-85323694; E-mail: wang_linchuan@163.com

#Contributed equally to this work.

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

Years	Testing Cases					Reactive Cases				Overall		
	Male	Female	Using 3 rd -generation	Using 4 th -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).

(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.

2.2. 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. The Cut-Off Index (COI) or Sample-to-Cutoff (S/CO) ≥ 1 was defined as reactive, and COI or S/CO < 1 was defined as non-reactive.

2.3. 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.

2.4. Definitions

According to the CDC guideline in China, the initially reactive case should be excluded from HIV infection if WB positive result is not observed at both of the first and 6 months follow-up tests, which should be defined as the false positive (FP) in the study. In addition, the subjects who were lost to follow-up, less than 18 months age or rejected to perform the WB test should be defined as the not-diagnosed (ND) cases.

2.5. 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.

3. RESULTS

3.1. 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 an overall new HIV/AIDS prevalence of 0.07% (469/622139). Due to 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 increase in the false-positive ratio (FPR). In addition, among the reactive cases for HIV screening, the not-diagnosed ratio (NDR) remained relatively stable (Rang: 9.09% to 15.0%), Table 1 & Fig. (1).

3.2. Features of False Positives (FP)

Of the 292 false positives from 2013 to 2018, most were male (55.82%) and 51—years old (67.81%), with a median age of 51 years (range: 16-86 years). 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).

3.3. The Demographic Constitution of New HIV/AIDS and Shift in the Epidemic

Among the new HIV/AIDS cases, the majority were Hans, males, people aged 21-50 years (76.97%), migrants, married, unemployed/informal employees, and sexual contact route (88.7%), with a male/female ratio of 5.9:1 and a median age of 39 years (range: 2-76 years). However, the new HIV/AIDS cases in the students (13.43%), -20 (6.18%), and 51—years age (16.84%) groups should be concerned. The new cases spread across Shaanxi province, of them, most were from Xi'an, Table 3. Among the 183 cases in Xi'an, 73.22% were from Changan (n=65), Yanta (n=40), and Beilin (n=29) districts, Fig (3B). In addition, Xianyang

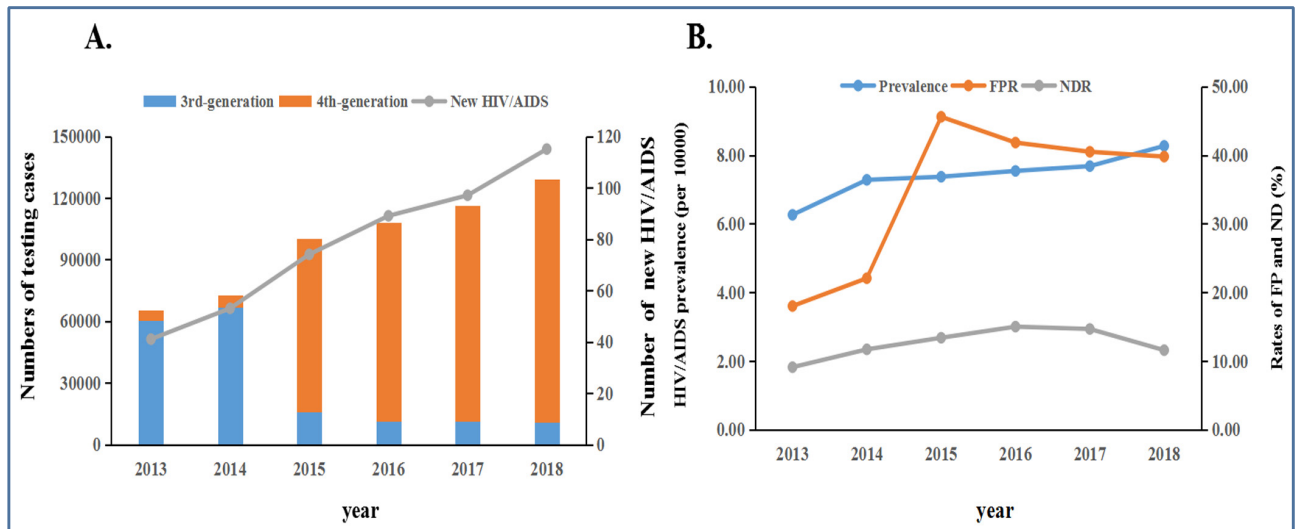


Fig. (1). Overall characteristics of HIV testing, (A) the number distributions of different screening tests and new HIV/AIDS cases from 2013 to 2018; (B) the shifts in HIV prevalence, false-positive ratio (FPR) and not-diagnosed ratio (NDR) from 2013 to 2018.

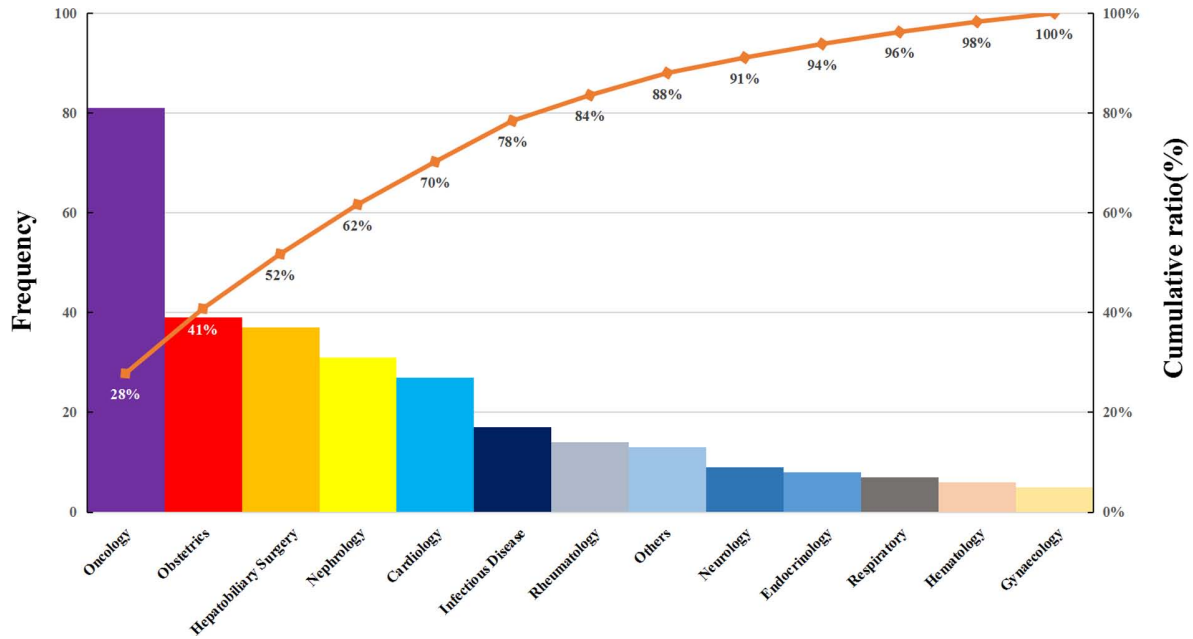


Fig. (2). The department distributions of the false-positive cases.

(n=54), Weinan (n=52), and Ankang (n=28) cities consisted of 63.81% of the cases in other areas in Shaanxi province, Fig. (3A). 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 shown 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).

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 overall HIV prevalence (0.07%) in the study still remained low and was also remarkably higher than that in Xi'an (0.01%) reported by CDC [22]; (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 mainly from Changan, Yanta, and Beilin districts, which may be related to the concentration of both the IDU and universities in these areas. Meanwhile, 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.

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

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 HIV/AIDS transmitting [23-30]. With the implementation of testing-based prevention for infectious diseases (HIV, HBV, HCV, and Syphilis) for pregnant women [31, 32], before operation, interventional examination, or treatment, the testing and confirmed cases for HIV increase yearly in China [5, 20, 33]. In addition, substantial intervention initiatives, such as "Action Plan on HIV/AIDS Prevention", "Four Free One Care" [5, 34-39], and "Prevention of Mother-to-Child Transmission (PMTCT) programme"[40], have been introduced since 2003. which resulted in an obvious decrease in the proportion of HIV/AIDS attributed to the vertical transmission in China

[41-45]. 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.

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

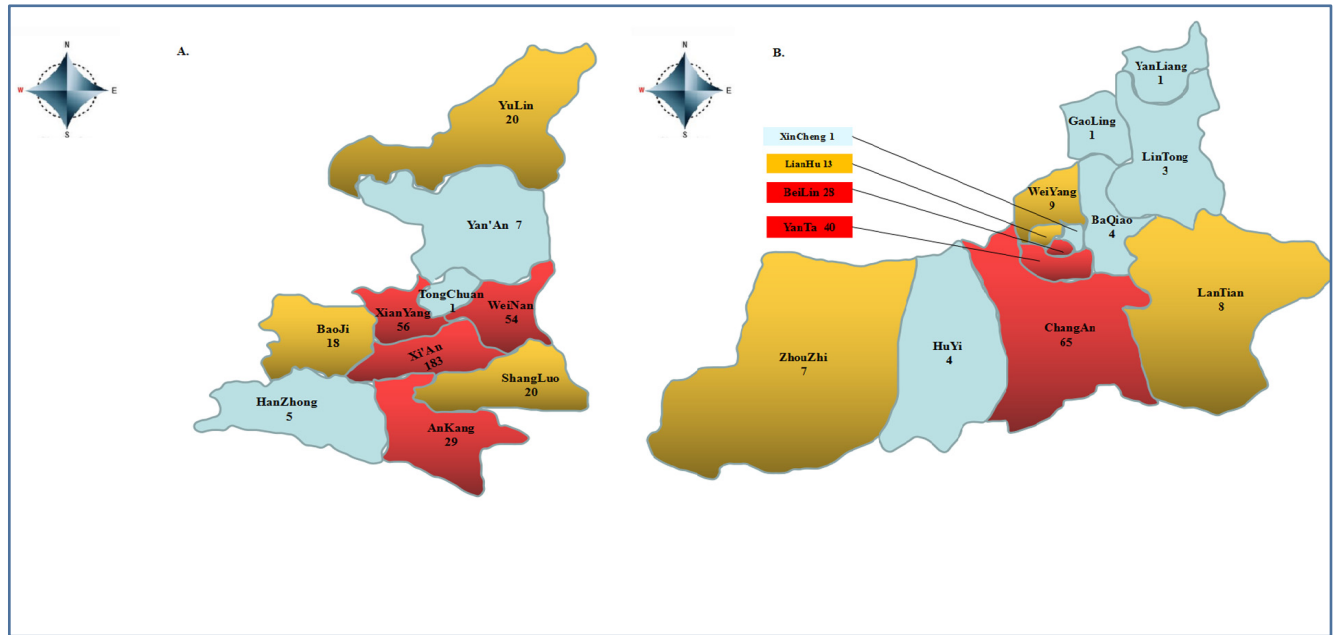


Fig. (3). Geographic distribution of the new HIV/AIDS cases in (A) Shaanxi province and (B) Xi'an city.

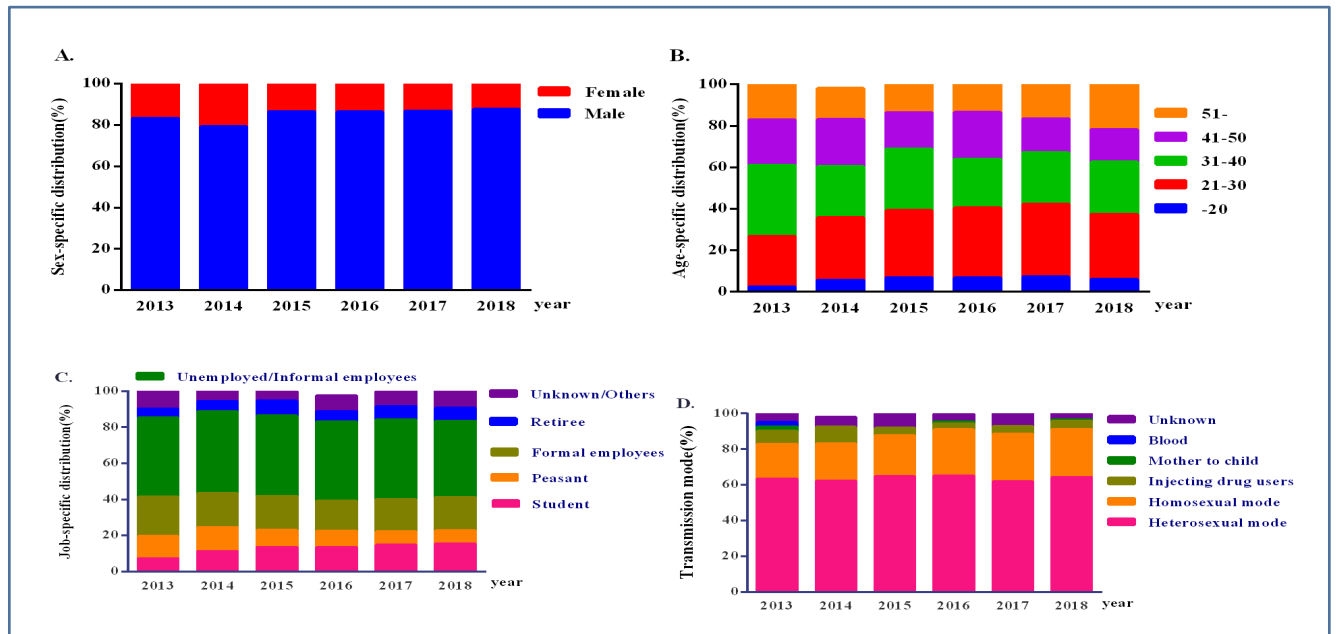


Fig. (4). Distributions of the new HIV/AIDS cases from 2013 to 2018 in terms of (A) Sex; (B) Age; (C) Job, and (D) Transmission mode.

China's HIV/AIDS epidemic began in the 1990s among injecting heroin users and commercial plasma donors [46-50]. Quite a few control policies, *i.e.*, "law against drug use" [51], "voluntary and compulsory detoxification" [52], "Methadone Maintenance Treatment (MMT) program" [53-57], and "commercial blood/plasma collection stations shut down and blood donors must be tested for HIV since 1995" [58], have been made and performed effectively in China, which led to the ratios of both IDU and blood routes among new infections decrease yearly [10, 59-61]. 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 [62-67]. In the study, the sexual contact was the most prominent route of HIV transmission in Xi'an, accounting for 88.7% of the cases, which was similar to other studies in Xi'an and other areas in China [6, 9, 10, 22].

Recently, it is notable that the HIV/AIDS epidemic in adolescents/students and older adults shows a significant increase in China [6, 10, 22, 68-70]. 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 13.43%, 6.18%, and 16.84%, 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 [9, 71, 72]. 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 (63.75%). However, the proportion of HIV cases attributed to females was only 14.50%. 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 [73-76]. In the study, 67.81% of FP cases were over 50 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%.

CONCLUSION

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, the 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.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

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.

HUMAN AND ANIMAL RIGHTS

No animals were used in this research. All humans research procedures were followed in accordance with the standards set forth in the Declaration of Helsinki principles of 1975, as revised in 2013 (<http://ethics.iit.edu/ecodes/node/3931>).

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

FUNDING

This study was supported by the grants from The First Affiliated Hospital of Xi'an Jiaotong University, Shaanxi Province, China (No. 2016MS-01), Natural Science Basic Research Program of Shaanxi Province, China (No. 2017JM8121, 2019JM-364) and Scientific and Technological Research Project of Xi'an, China [No. 2019114613YX001SF043(3)].

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

ACKNOWLEDGEMENTS

Declared none.

REFERENCES

- [1] Schaeffer AJ. The AIDS epidemic--considerations for the 21st century. *J Urol* 2000; 164(1): 263-4. PMID: 10896519
- [2] Samanta GP. Analysis of a Nonautonomous HIV/AIDS Epidemic Model with Distributed Time Delay. *Math Model Anal* 2010; 15(3): 327-47. <http://dx.doi.org/10.3846/1392-6292.2010.15.327-347>
- [3] Bera S P, Maiti A, Samanta G P. A delay dynamic model for HIV infected immune response. *J App Math Info* 2015; 559-78. <http://dx.doi.org/10.14317/jami.2015.559>
- [4] Yi Z, Wu Z. Control of Aids Epidemic in China *Bulletin of the Chinese Academy of Sciences* 2000; 2: 106-11.
- [5] Wu Z, Sullivan SG, Wang Y, Rotheram-Borus MJ, Detels R. Evolution of China's response to HIV/AIDS. *Lancet* 2007; 369(9562): 679-90. [http://dx.doi.org/10.1016/S0140-6736\(07\)60315-8](http://dx.doi.org/10.1016/S0140-6736(07)60315-8) PMID: 17321313
- [6] Yan Y, Wu S, Chen L, et al. Shift in HIV/AIDS Epidemic in Southeastern China: A Longitudinal Study from 1987 to 2015. *Int J Environ Res Public Health* 2016; 13(8): 794-808. <http://dx.doi.org/10.3390/ijerph13080794> PMID: 27509511
- [7] Kaufman J, Jing J. China and AIDS--the time to act is now. *Science* 2002; 296(5577): 2339-40. <http://dx.doi.org/10.1126/science.1074479> PMID: 12089428
- [8] Zeng M. Driving out the spectre of AIDS that has entered the country: current situation of AIDS in China. *MingPao Yue Kan* 1992; 27(6): 20-2.
- [9] Sun W, Wu M, Qu P, Lu C, Wang L. Quality of life of people living with HIV/AIDS under the new epidemic characteristics in China and the associated factors. *PLoS One* 2013; 8(5): e64562. <http://dx.doi.org/10.1371/journal.pone.0064562> PMID: 23741340
- [10] Huang MB, Ye L, Liang BY, et al. Characterizing the HIV/AIDS Epidemic in the United States and China. *Int J Environ Res Public Health* 2015; 13(1): 30.
- [11] Ministry of Health of the People's Republic of China. 2011 Estimates for the HIV/AIDS Epidemic in China. Beijing, China: Ministry of Health 2011.
- [12] Tang Q, Lu H. HIV/AIDS responses in China should focus on the impact of global integration. *Biosci Trends* 2018; 12(5): 507-9. <http://dx.doi.org/10.5582/bst.2018.01269> PMID: 30473559
- [13] Jia Z, Ruan Y, Lu Z. HIV incidence and mortality in China. *Lancet* 2015; 385(9977): 1510.

- [http://dx.doi.org/10.1016/S0140-6736\(15\)60753-X](http://dx.doi.org/10.1016/S0140-6736(15)60753-X) PMID: 25933281
- [14] Yang S, Wu J, Ding C, *et al.* Epidemiological features of and changes in incidence of infectious diseases in China in the first decade after the SARS outbreak: an observational trend study. *Lancet Infect Dis* 2017; 17(7): 716-25. [http://dx.doi.org/10.1016/S1473-3099\(17\)30227-X](http://dx.doi.org/10.1016/S1473-3099(17)30227-X) PMID: 28412150
- [15] National Center for AIDS/STD Control and Prevention. National AIDS and STD epidemic in the third quarter of 2018. *Chinese J AIDS STD* 2018; 24(11): 1075.
- [16] Wang L, Xiao Y, Tian XD, Ruan JX, Chen W, Yu Y. HIV infection in Xi'an, China: epidemic characterization, risk factors to false positives and potential utility of the sample-to-cutoff index to identify true positives using Architect HIV Ag/Ab combo. *Antimicrob Resist Infect Control* 2019; 8(1): 9. <http://dx.doi.org/10.1186/s13756-019-0463-0> PMID: 30651975
- [17] Zhang Y, Xiao Q, Zhou L, *et al.* The AIDS epidemic and economic input impact factors in Chongqing, China, from 2006 to 2012: a spatial-temporal analysis. *BMJ Open* 2015; 5(3): e006669. <http://dx.doi.org/10.1136/bmjopen-2014-006669> PMID: 25818270
- [18] Zhang X, Tang W, Li Y, *et al.* The HIV/AIDS epidemic among young people in China between 2005 and 2012: results of a spatial temporal analysis. *HIV Med* 2017; 18(3): 141-50. <http://dx.doi.org/10.1111/hiv.12408> PMID: 27552922
- [19] Yu ES, Xie Q, Zhang K, Lu P, Chan LL. HIV infection and AIDS in China, 1985 through 1994. *Am J Public Health* 1996; 86(8): 1116-22. http://dx.doi.org/10.2105/AJPH.86.8_Pt_1.1116 PMID: 8712271
- [20] Liu Z, Shi O, Yan Q, *et al.* Changing epidemiological patterns of HIV and AIDS in China in the post-SARS era identified by the nationwide surveillance system. *BMC Infect Dis* 2018; 18(1): 700. <http://dx.doi.org/10.1186/s12879-018-3551-5> PMID: 30587142
- [21] National Center for AIDS/STD Control and Prevention. Update on the AIDS/STD epidemic in China and main response in control and prevention in December 2015. *Chinese J AIDS STD* 2016; 22(2): 69.
- [22] Long X, Jiang-Bo LI. Epidemiological characteristics of HIV/AIDS people aged above 50 years old in Xi'an, 2011-2015. *Mod Prev Med* 2016; 43(3): 4248-50.
- [23] Li W, Jiang J, Su J, *et al.* Commercial Sexual Behaviors Among Male Rural-to-Urban Migrants in Western China: Implications for HIV Prevention. *Asia Pac J Public Health* 2017; 29(5): 388-400. <http://dx.doi.org/10.1177/1010539517709029> PMID: 28523944
- [24] Lurie MN, Williams BG, Zuma K, *et al.* The impact of migration on HIV-1 transmission in South Africa: a study of migrant and nonmigrant men and their partners. *Sex Transm Dis* 2003; 30(2): 149-56. <http://dx.doi.org/10.1097/00007435-200302000-00011> PMID: 12567174
- [25] Samanta GP. Analysis of a nonautonomous hiv/aids model. *Math Model Nat Phenom* 2010; 5(6): 70-95. <http://dx.doi.org/10.1051/mmnp/20105604>
- [26] Samanta GP. Permanence and extinction of a nonautonomous HIV/AIDS epidemic model with distributed time delay. *Nonlinear Anal Real World Appl* 2011; 12(2): 1163-77. <http://dx.doi.org/10.1016/j.nonrwa.2010.09.010>
- [27] Sharma S, Samanta GP. Dynamical Behaviour of an HIV/AIDS Epidemic Model. *Differential Equations and Dynamical Systems* 2014; 22(4): 369-95. <http://dx.doi.org/10.1007/s12591-013-0173-7>
- [28] Saha S, Samanta GP. Modelling and optimal control of HIV/AIDS prevention through PrEP and limited treatment. *Physica A* 2019; 280-307. <http://dx.doi.org/10.1016/j.physa.2018.10.033>
- [29] Ministry of Health of China/UNAIDS/WHO. 2009 Update on the HIV/AIDS Epidemic and Response in China. Accessed on 18 June 2010. Available online: <http://wsb.moh.gov.cn/mohjbyfkzj/s3586/201009/48858.shtml>
- [30] Tiruneh K, Wasie B, Gonzalez H. Sexual behavior and vulnerability to HIV infection among seasonal migrant laborers in Metema district, northwest Ethiopia: a cross-sectional study. *BMC Public Health* 2015; 15: 122. <http://dx.doi.org/10.1186/s12889-015-1468-0> PMID: 25885580
- [31] Ministry of Health of China. Protocol for prevention of mother-to-child transmission of HIV, syphilis and Hepatitis B. Beijing: Ministry of Health 2011.
- [32] Zeng H, Chow EPF, Zhao Y, *et al.* Prevention of mother-to-child HIV transmission cascade in China: a systematic review and meta-analysis. *Sex Transm Infect* 2016; 92(2): 116-23. <http://dx.doi.org/10.1136/sextrans-2014-051877> PMID: 25935929
- [33] Sun X, Lu F, Wu Z, *et al.* Evolution of information-driven HIV/AIDS policies in China. *Int J Epidemiol* 2010; 39(Suppl. 2): ii4-ii13. <http://dx.doi.org/10.1093/ije/dyq217> PMID: 21113036
- [34] Rou K, Sullivan SG, Liu P, Wu Z. Scaling up prevention programmes to reduce the sexual transmission of HIV in China. *Int J Epidemiol* 2010; 39(Suppl. 2): ii38-46. <http://dx.doi.org/10.1093/ije/dyq211> PMID: 21113035
- [35] Zhang KL, Detels R, Liao S, Cohen M, Yu DB. China's HIV/AIDS epidemic: continuing challenges. *Lancet* 2008; 372(9652): 1791-3. [http://dx.doi.org/10.1016/S0140-6736\(08\)61357-4](http://dx.doi.org/10.1016/S0140-6736(08)61357-4) PMID: 18930521
- [36] Yi H, Lau JTF, Yi H, Lau JTF. Emerging issues, challenges and aspirations in the HIV/AIDS epidemic in China. *Public Health* 2011; 125(5): 257-9. <http://dx.doi.org/10.1016/j.puhe.2011.01.012> PMID: 21349560
- [37] Gill B, Okie S. China and HIV - a window of opportunity. *N Engl J Med* 2007; 356(18): 1801-5. <http://dx.doi.org/10.1056/NEJMp078010> PMID: 17476005
- [38] Xue B. HIV/AIDS policy and policy evolution in China. *Int J STD AIDS* 2005; 16(7): 459-64. <http://dx.doi.org/10.1258/0956462054308477> PMID: 16004623
- [39] Wu Z, Wang Y, Detels R, Rotheram-Borus MJ. China AIDS policy implementation: reversing the HIV/AIDS epidemic by 2015. *Int J Epidemiol* 2010; 39(Suppl. 2): ii1-3. <http://dx.doi.org/10.1093/ije/dyq220> PMID: 21113031
- [40] Wang AL, Qiao YP, Wang LH, *et al.* Integrated prevention of mother-to-child transmission for human immunodeficiency virus, syphilis and hepatitis B virus in China. *Bull World Health Organ* 2015; 93(1): 52-6. <http://dx.doi.org/10.2471/BLT.14.139626> PMID: 25558108
- [41] Jia Z, Wang L, Chen RY, *et al.* Tracking the evolution of HIV/AIDS in China from 1989-2009 to inform future prevention and control efforts. *PLoS One* 2011; 6(10): e25671. <http://dx.doi.org/10.1371/journal.pone.0025671> PMID: 21998679
- [42] Gao W, Li Z, Li Y, Qiao X. Sexual Practices and the Prevalence of HIV and Syphilis among Men Who Have Sex with Men in Lanzhou, China. *Jpn J Infect Dis* 2015; 68(5): 370-5. <http://dx.doi.org/10.7883/yoken.JJID.2013.477> PMID: 25766603
- [43] Jiang Y, Qiu M, Zhang G, *et al.* Quality assurance in the HIV/AIDS laboratory network of China. *Int J Epidemiol* 2010; 39(Suppl 2): ii72-8.
- [44] Wu Z, Rou K, Cui H. The HIV/AIDS epidemic in China: History current strategies and future challenges. *AIDS Edu Prev* 2004; 16(3 Suppl A): 7-17.
- [45] Watts J. Sex, drugs, and HIV/AIDS in China. *Lancet* 2008; 371(9607): 103-4. [http://dx.doi.org/10.1016/S0140-6736\(08\)60087-2](http://dx.doi.org/10.1016/S0140-6736(08)60087-2) PMID: 18196617
- [46] Zhang KI KL, Ma SJ. Epidemiology of HIV in China. *BMJ* 2002; 324(7341): 803-4. <http://dx.doi.org/10.1136/bmj.324.7341.803> PMID: 11934762
- [47] Zheng X, Tian C, Choi KH, *et al.* Injecting drug use and HIV infection in southwest China. *AIDS* 1994; 8(8): 1141-7. <http://dx.doi.org/10.1097/00002030-199408000-00017> PMID: 7986413
- [48] Yao J. Yunnan: China's anti-drug outpost. *BeijingRev* 1991; 34(34): 20-5.
- [49] Zheng X, Tian C, Zhang G, *et al.* HIV risk behaviors but absence of infection among drug users in detoxification centers outside Yunnan province, China, 1993. *AIDS* 1995; 9(8): 959-63. <http://dx.doi.org/10.1097/00002030-199508000-00020> PMID: 7576334
- [50] Zheng X, Zhang J, Qu S. Cohort study of HIV infection among drug users in Ruili and other counties in Yunnan Province, China. *Zhonghua Liu Xing Bing Xue Za Zhi* 1994; 15(1): 2-5. PMID: 8082135

- [51] Standing Committee of the National People's Congress. Decision on the prohibition of narcotic drugs Beijing: Standing Committee of the National People's Congress 1990.
- [52] Ministry of Public Security. Administration of compulsory detoxification at rehabilitation centres. Beijing: Ministry of Public Security 2000. Document number 49.
- [53] Lin C, Wu Z, Detels R. Family support, quality of life and concurrent substance use among methadone maintenance therapy clients in China. *Public Health* 2011; 125(5): 269-74. <http://dx.doi.org/10.1016/j.puhe.2011.01.009> PMID: 21414646
- [54] Lin C, Cao X, Li L. Psychoactive Substance Use among Methadone Maintenance Therapy Clients in China. *Int J Ment Health Addict* 2017; 15(4): 801-11. <http://dx.doi.org/10.1007/s11469-017-9758-7> PMID: 28761409
- [55] Wang M, Mao W, Zhang L, *et al.* Methadone maintenance therapy and HIV counseling and testing are associated with lower frequency of risky behaviors among injection drug users in China. *Subst Use Misuse* 2015; 50(1): 15-23. <http://dx.doi.org/10.3109/10826084.2014.957768> PMID: 25295376
- [56] Wan D. Partnership Status, Continued Drug Use and Treatment Adherence among Newly Enrolled Methadone Maintenance Therapy Patients in China. *Dissertations & Theses-Gradworks* 2012.
- [57] Li L, Liang LJ, Lin C, Feng N, Wu Z. Comparison Between Urinalysis Results and Self-Reported Heroin Use Among Patients Undergoing Methadone Maintenance Treatment in China. *Subst Use Misuse* 2017; 52(10): 1307-14. <http://dx.doi.org/10.1080/10826084.2016.1276598> PMID: 28346039
- [58] State Council of People's Republic of China. Regulations for the management of blood products. Beijing: State Council 1996. Document number 208.
- [59] Zhang L, Chow EPF, Jing J, *et al.* HIV prevalence in China: integration of surveillance data and a systematic review. *Lancet Infect Dis* 2013; 13(11): 955-63. [http://dx.doi.org/10.1016/S1473-3099\(13\)70245-7](http://dx.doi.org/10.1016/S1473-3099(13)70245-7) PMID: 24107261
- [60] Meng X, Zou H, Beck J, *et al.* Trends in HIV prevalence among men who have sex with men in China 2003-09: a systematic review and meta-analysis. *Sex Health* 2013; 10(3): 211-9. <http://dx.doi.org/10.1071/SH12093> PMID: 23611402
- [61] Chen XS, Liang GJ, Wang QQ, *et al.* HIV prevalence varies between female sex workers from different types of venues in southern China. *Sex Transm Dis* 2012; 39(11): 868-70. <http://dx.doi.org/10.1097/OLQ.0b013e318264c3ba> PMID: 23064536
- [62] Dou Z, Chen RY, Xu J, *et al.* Changing baseline characteristics among patients in the China National Free Antiretroviral Treatment Program, 2002-09. *Int J Epidemiol* 2010; 39(Suppl 2(suppl 2)): ii56.
- [63] Li X, Zhang L, Stanton B, Fang X, Xiong Q, Lin D. HIV/AIDS-related sexual risk behaviors among rural residents in China: potential role of rural-to-urban migration. *AIDS Educ Prev* 2007; 19(5): 396-407. <http://dx.doi.org/10.1521/aeap.2007.19.5.396> PMID: 17967110
- [64] Wu JQ, Wang KW, Zhao R, *et al.* Male rural-to-urban migrants and risky sexual behavior: a cross-sectional study in Shanghai, China. *Int J Environ Res Public Health* 2014; 11(3): 2846-64. <http://dx.doi.org/10.3390/ijerph110302846> PMID: 24619119
- [65] Yang X, Li S, Attané I, Feldman MW. Commercial sex behaviours among involuntary male bachelors: findings from a survey of migrants in Xi'an, China. *J Public Health (Oxf)* 2015; 37(2): 305-12. <http://dx.doi.org/10.1093/pubmed/dfu047> PMID: 25104838
- [66] Cai R, Richardus JH, Looman CW, de Vlas SJ. Trends in high-risk sexual behaviors among general population groups in China: a systematic review. *PLoS One* 2013; 8(11): e79320. <http://dx.doi.org/10.1371/journal.pone.0079320> PMID: 24236121
- [67] Zhu GR, Ji CY, Yang XH. Relationship between migration and HIV risky behavior: a comparative study of returning migrants and non migrants based on rural out-of-school youth in Jilin, China. *Biomed Environ Sci* 2015; 28(6): 429-36. PMID: 26177903
- [68] Xing J, Li YG, Tang W, *et al.* HIV/AIDS epidemic among older adults in China during 2005-2012: results from trend and spatial analysis. *Clin Infect Dis* 2014; 59(2): e53-60. <http://dx.doi.org/10.1093/cid/ciu214> PMID: 24700658
- [69] Liu H, Lin X, Xu Y, Chen S, Shi J, Morisky D. Emerging HIV epidemic among older adults in Nanning, China. *AIDS Patient Care STDS* 2012; 26(10): 565-7. <http://dx.doi.org/10.1089/apc.2012.0227> PMID: 22984779
- [70] Lu L, Jia M, Ma Y, *et al.* The changing face of HIV in China. *Nature* 2008; 455(7213): 609-11. <http://dx.doi.org/10.1038/455609a> PMID: 18833270
- [71] Huang ZJ, He N, Nehl EJ, *et al.* Social network and other correlates of HIV testing: findings from male sex workers and other MSM in Shanghai, China. *AIDS Behav* 2012; 16(4): 858-71. <http://dx.doi.org/10.1007/s10461-011-0119-4> PMID: 22223298
- [72] Li R, Pan X, Ma Q, *et al.* Prevalence of prior HIV testing and associated factors among MSM in Zhejiang Province, China: a cross-sectional study. *BMC Public Health* 2016; 16(1): 1152. <http://dx.doi.org/10.1186/s12889-016-3806-2> PMID: 27832761
- [73] Liu P, Shi Z, Wang C, *et al.* The false-positive and false-negative predictive value of HIV antibody test in the Chinese population. *J Med Screen* 2008; 15(2): 72-5. <http://dx.doi.org/10.1258/jms.2008.007082> PMID: 18573774
- [74] Caiyun L, Kai G, Yan L, *et al.* Analysis of specimens testing positive in an HIV antibody screening test and negative in a confirmatory test. *J Path Biol* 2010; 5(4): 256-258. Available from: http://en.cnki.com.cn/Article_en/CJFDTotals/ZISC201004006.htm
- [75] Liu P, Jackson P, Shaw N, Heysell S. Spectrum of false positivity for the fourth generation human immunodeficiency virus diagnostic tests. *AIDS Res Ther* 2016; 13(1): 1. <http://dx.doi.org/10.1186/s12981-015-0086-3> PMID: 26734067
- [76] Ellen AM, Beavis KG, Angella CK, *et al.* A Series of False-Positive Fourth-Generation Rapid Human Immunodeficiency Virus (HIV) Tests in an Urban Labor and Delivery Setting. *Open Forum Infect Dis* 2016; 3(suppl_1): 524.