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在线全文

艾滋病住院初治患者HIV-1基因亚型及传播性耐药现状分析*

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【摘要】 目的 分析感染科艾滋病住院初治患者HIV-1基因亚型分布特征、传播性耐药（transmitted drug resistance, TDR）现状及其影响因素。**方法** 纳入2020年1月–2022年12月期间在成都市公共卫生临床医疗中心感染科住院并确诊的初治艾滋病患者，收集患者抗病毒治疗（antiretroviral therapy, ART）前的血液样本，采用in-house法进行HIV基因扩增、测序，系统进化树分析HIV-1基因亚型，HIV耐药数据库在线比对分析耐药突变位点、耐药种类、耐药程度，进行HIV-1基因亚型分布特征和TDR发生情况及其影响因素分析。**结果** 共收集213例患者的血样，HIV基因扩增成功率83.10%（177/213），共检出10种基因亚型，以CRF07_BC最常见（43.50%，77/177），其次为CRF01_AE（37.85%），独特重组亚型（unique recombinant forms, URFs）较少（8.47%），其他亚型10.17%；这4种HIV-1基因亚型仅在不同年龄的分布差异有统计学意义（*P*=0.024），进一步分析发现仅CRF01_AE和URFs在年龄为30～50岁和年龄>50岁的分布差异有统计学意义，URFs在年龄为30～50岁人群占比较高（*P*=0.008）。CRF07_BC、CRF01_AE、URFs、其他亚型耐药发生率分别为6.49%、8.96%、13.33%、5.56%，差异无统计学意义（*P*>0.05）；TDR总发生率6.57%，非核苷类逆转录酶抑制剂（non-nucleoside reverse transcriptase inhibitors, NNRTIs）TDR发生率5.16%，突变位点主要为V179D/E、E138A/G、V106M/I、Y181C，核苷类逆转录酶抑制剂（nucleoside reverse transcriptase inhibitors, NRTIs）TDR发生率1.88%，突变位点主要为M184V，1例患者发生NNRTIs、NRTIs双重耐药；4.23%高度耐药，0.47%中度耐药，1.88%低度耐药；本研究未发现TDR在不同年份、人口学特征、感染途径、基线状况、机会性感染方面的差异有统计学意义（*P*>0.05）。**结论** 艾滋病住院初治患者HIV-1基因亚型复杂、多样，TDR总发生率较高，需加强TDR监测，以优化ART治疗、减少耐药传播。

【关键词】 获得性免疫缺陷综合征 基因亚型 传播性耐药

Analysis of HIV-1 Subtypes and Transmitted Drug Resistance in Hospitalized Treatment-Native Patients With AIDS

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【Abstract】 Objective To investigate the distribution characteristics of HIV-1 subtypes, the status of transmitted drug resistance (TDR), and the influencing factors of TDR in treatment-naive patients with AIDS who are hospitalized. **Methods** Treatment-naive patients with AIDS who were admitted to the Infectious Disease Department, Public Health Clinical Center of Chengdu between January 2020 and December 2022 were enrolled in the study. The diagnosis and confirmation diagnosis of all the subjects were made at the same hospital. Blood samples were collected from the subjects before antiretroviral therapy (ART). The in-house method was used for HIV gene amplification and sequencing. A phylogenetic tree was constructed to analyze the HIV-1 subtypes. The Stanford HIV Drug Resistance Database was used to conduct an online comparative analysis of the drug resistance mutation sites and to determine the types and levels of drug resistance. The distribution characteristics of HIV-1 subtypes, the occurrence of TDR, and the influencing factors of TDR were analyzed. **Results** A total of 213 patients were included in the study and their blood samples were collected. HIV-1 subtypes were successfully amplified in 83.10% (177/213) of the subjects. Ten HIV subtypes were identified, with CRF07_BC being the most common subtypes, accounting for 43.50% (77/177), which was followed by CRF01_AE at 37.85%. Unique recombinant forms (URFs) were relatively uncommon, accounting for 8.47%. The other subtypes accounted for 10.17%. These 4 categories of HIV-1 subtypes were distributed with statistically significant differences in different age groups (*P*=0.024). Further analysis revealed significant differences in the distribution of the HIV-1 subtypes of CRF01_AE and URFs between the groups of patients aged 30-50 years and those over 50. In addition, URFs accounted for a higher proportion in patients aged 30 to 50 years (*P*=0.008). The incidences of TDR were 6.49%, 8.96%, 13.33%, and 5.56% for CRF07_BC, CRF01_AE, URFs, and other subtypes, respectively, showing

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no significant difference (P>0.05). The overall TDR was 6.57%. The TDR for non-nucleoside reverse transcriptase inhibitors (NNRTIs) was 5.16%, and the main mutation sites were V179D/E, E138A/G, V106M/I, and Y181C. The TDR for nucleoside reverse transcriptase inhibitors (NRTIs) was 1.88%, and the main mutation site was M184V. One patient was found to be resistant to both NNRTIs and NRTIs. The highly resistant rate was 4.23%, moderate resistance was 0.47%, and low resistance was 1.88%. No significant effects of the specific years, demographic characteristics, transmission route, baseline condition, and opportunistic infections on TDR were found in this study (P>0.05). **Conclusions** The HIV-1 subtypes are diverse and complex in treatment-naive patients with AIDS who were hospitalized. The overall prevalence of TDR is relatively high. It is necessary to strengthen HIV drug resistance testing to optimize ART treatment and reduce the risk of drug resistance transmission.

【Key words】 Acquired immunodeficiency syndrome HIV-1 subtypes Transmitted drug resistance

随着抗病毒治疗(antiretroviral therapy, ART)的广泛使用, HIV耐药不可避免[1]。HIV耐药分为获得性耐药、传播性耐药(transmitted drug resistance, TDR)和治疗前耐药[2], TDR将增加ART失败风险和患者死亡风险, 进一步导致耐药毒株的传播, 增加医护成本, 对艾滋病防控造成重大挑战[3]。进行TDR监测非常重要, 可为制定有效的ART方案提供重要信息, 减少HIV耐药发生, 并制定合理的公共卫生防治战略。然而, 在资源有限地区并未常规开展TDR检测, TDR的发生率在中国各地区差异较大[4], 有关TDR的影响因素各研究报道结果不一致。目前关于本地区TDR的研究报道较少, 艾滋病住院患者由于病情复杂、合并多种疾病及机会性感染, 其HIV-1基因亚型及TDR是否存在特异性, 尚无相关报道。因此本研究调查分析近3年艾滋病住院患者HIV-1基因亚型分布特征、TDR发生情况及影响因素, 为本地有效开展艾滋病防治工作提供参考依据。

1 资料与方法

1.1 研究对象

入选标准: ① 2020年1月–2022年12月期间在成都市公共卫生临床医疗中心感染科住院并确诊为艾滋病的患者, 艾滋病诊断标准参考《中国艾滋病诊疗指南(2018版)》[5]; ②患者启动ART前签署知情同意书, 自愿进行HIV-1基因亚型及耐药检测; ③年龄>18岁, ④基线HIV RNA≥1 000 copies/mL; ⑤初治患者。排除标准: ①未曾服用过HIV暴露前预防药物或暴露后预防药物; ②合并乙肝患者曾服用过核苷类似物治疗; ③民族、婚姻状况、户籍、感染途径、基线HIV RNA、CD4等资料不详; ④不符合入选标准中任一项。该研究已经通过成都市公共卫生临床医疗中心伦理委员会审批(批准号20180129)。

1.2 方法

1.2.1 HIV-1 RNA提取及测序

抽取患者5 ~ 10 mL外周静脉血, 进行离心留取血浆。使用中山大学达安基因股份有限公司生产的核酸提取试剂盒提取HIV RNA, 并将RNA反转录为cDNA, in-house法进行产物扩增后进行纯化处理, ABI3730测序仪进行HIV基因测序, BioEdit对测序成功的序列进行编辑、拼接和校正, Contig-分析序列, 每轮34个循环, 共2轮。

1.2.2 HIV-1基因亚型分型

MEGA 6.0软件构建Neighbor-Joining系统进化树, Distance Model模型选择Kimura 2-parameter, Bootstrap Replicates设置1 000, 判断基因亚型。

1.2.3 HIV-1耐药分析

将测序结果导入HIV药物检测系统, 得到完整fasta格式序列, 美国斯坦福大学HIV耐药数据库(http://hivdb.stanford.edu/)在线分析耐药突变位点、耐药种类、耐药程度。

1.3 统计学方法

建立Excel数据库收集、录入相关资料, SPSS 26.0进行统计学分析, 计量资料进行正态分布检验, 满足正态分布用$\bar{x}\pm s$表示, 计数资料采用例数、构成比、率表示; 4种不同基因亚型组之间在人口学特征、基线情况、机会性感染等方面的差异比较采用χ^2检验或Fisher精确概率法; 对影响TDR发生的因素, 先进行单因素分析, 将P< 0.1的因素纳入模型进行多因素logistic回归分析。α= 0.05。

2 结果

2.1 基本情况

共纳入213例患者, 年龄范围19 ~ 90岁, 平均(45.42±16.23)岁; 平均住院(29.69±15.59) d, 以男性、汉族为主, 未婚、本省户籍、异性传播、高基线HIV-RNA、低基线CD4、合并多种机会性感染的患者占比较高, 详见表1。

2.2 HIV-1基因亚型分布特征

扩增成功率83.10%(177/213), 检出10种基因亚型, 以CRF07_BC最常见(43.50%, 77/177), 其次为CRF01_AE(37.85%, 67/177), URFs较少(8.47%, 15/177), 10.17%

表 1　2020–2022年213例住院艾滋病患者基本情况及HIV-1基因亚型分布

Table 1　Basic information and HIV-1 genetic subtype distribution of 213 hospitalized patients with AIDS from 2020 to 2022

Variable		Total/case	Successfully amplified/case	HIV-1 major genotype/case				χ^2/Fisher	*P*
				CRF07_BC (*n*=77)	CRF01_AE (*n*=67)	URFs (*n*=15)	Others (*n*=18)		
Year	2020	57	38	14	15	2	7	5.35[a]	0.499
	2021	65	54	23	20	7	4		
	2022	91	85	40	32	6	7		
Age/yr.	<30	45	37	12	17	3	5	14.14[a]	0.024
	30-50	86	72	35	18	10	9		
	>50	82	68	30	32	2	4		
Sex	Female	31	26	12	11	1	2	0.81[a]	0.886
	Male	182	151	65	56	14	16		
Ethnicity	Ethnic minorities	11	9	6	2	1	0	2.38[a]	0.454
	Han	202	168	71	65	14	18		
Marital status	Single	80	69	28	24	7	10	2.954	0.397
	Married	133	108	49	43	8	8		
Registered residence	Chengdu	90	75	34	31	5	5	5.00[a]	0.532
	Sichuan province	106	85	36	31	9	9		
	Outside Sichuan province	17	17	7	5	1	4		
HIV transmission route	Heterosexual transmission	148	119	51	49	8	11	4.98[a]	0.497
	Homosexual transmission	58	52	22	17	7	6		
	Injecting drug use	7	6	4	1	0	1		
Baseline HIV-1 RNA/(copies/mL)	⩾100 000	154	131	56	50	10	15	1.32[a]	0.742
	<100 000	59	46	21	17	5	3		
Baseline CD4/(cells/μL)	<50	123	103	39	42	10	12	3.331	0.350
	⩾50	90	74	38	25	5	6		
Number of opportunistic infections	⩽1	39	34	19	10	1	4	3.66[a]	0.302
	⩾2	174	143	58	57	14	14		
Drug resistance	Yes	14	14	5	6	2	1	1.34[a]	0.779
	No	199	163	72	61	13	17		

15 cases of URFs included 11 cases of B+C, 3 cases of B+CRF01-AE, and 1 case of B+CRF67-01B. The others cases included 7 cases of B, 4 cases of CRF08-BC, 3 cases of C, 3 cases of CRF55-01B, and 1 case of CRF59-01B. [a] Fisher's exact test.

(18/177)为其他亚型。4种HIV-1基因亚型仅在不同年龄的分布差异有统计学意义(P= 0.024), 对基因亚型和年龄分别进行卡方检验的多重分析比较发现: 基因亚型仅CRF01_AE和URFs在年龄为30 ~ 50岁和年龄> 50岁的分布差异有统计学意义, URFs在年龄为30 ~ 50岁人群占比较高(P= 0.008)。详见表1。

2.3　HIV-1 TDR分析

CRF07_BC、CRF01_AE、URFs、其他亚型耐药发生率分别为6.49%、8.96%、13.33%、5.56%, 差异无统计学意义(P> 0.05); 2020–2022年TDR发生率分别为1.75%(1/57)、6.15%(4/65)、9.89%(9/91), 3年TDR总发生率6.57%(14/213)。耐药种类: 以非核苷类逆转录酶抑制剂(non-nucleoside reverse transcriptase inhibitors, NNRTIs)为主(5.16%, 11/213), 其次为核苷类逆转录酶抑制剂(nucleoside reverse transcriptase inhibitors, NRTIs)(1.88%, 4/213), 其中1例患者发生NNRTIs、NRTIs双重耐药; 未发现蛋白酶抑制剂(protease inhibitor, PIs)及整合酶链转移酶抑制剂(integrase strand transfer inhibitors, INTIs)相关耐药。耐药程度: 高度耐药4.23%(9/213), 中度耐药0.47%(1/213), 低度耐药1.88%(4/213)。单因素回归分析

未发现TDR在人口学特征(年龄、性别、民族、婚姻状况、居住地)、基线状况(基线HIV-1 RNA、基线CD4水平)、机会性感染方面的差异有统计学意义($P>0.1$)。单因素回归分析筛选出年份、感染途径进入多因素回归分析($P<0.1$),但后者显示这两个因素与TDR发生无关($P>0.05$, 表2)。

2.4 耐药突变位点与TDR关系

NNRTIs突变位点:V179D/E(5/11)、E138A/G(4/11)、Y181C(2/11)、V106M/I(2/11)、G190A(1/11)、K103N(1/11)、Y188D(1/11),依法韦仑(EFV)、奈韦拉平(NVP)耐药发生率相同,均为4.69%(10/213);NRTIs突变位点:M184V(3/4)、M41L(2/4)、K65R(1/4)、K70T(1/4),恩曲他滨(FTC)、拉米夫定(3TC)高度耐药主要与M184V相关(3/4)。7例为复合突变,具体突变位点及耐药情况详见表3。

表 2 HIV-1 TDR发生情况及影响因素的logistic回归分析

Table 2 Logistic regression analysis of HIV-1 transmission drug resistance (TDR) and the influencing factors

Variable		Total/n=213, case	Drug resistance/ n=14, case	Univariate analysis		Multivariate analysis	
				OR (95% CI)	P	OR (95% CI)	P
Year	2020	57	1	1.000		1.000	
	2021	65	4	3.672 (0.398, 33.849)	0.251	3.921 (0.420, 36.612)	0.231
	2022	91	9	6.222 (0.767, 50.501)	0.087	7.069 (0.856, 58.342)	0.069
HIV transmission route	Heterosexual transmission	148	7	1.000		1.000	
	Homosexual transmission	58	7	2.745 (0.918, 8.210)	0.071	3.734 (0.974, 14.311)	0.055
	Injecting drug use	7	0	0	0.999	0	0.999

OR: odds ratio; CI: confidence interval.

表 3 14例TDR患者耐药位点突变情况

Table 3 Transmitted drug resistance mutations sites of 14 patients

Sequence	Year	HIV transmission route	HIV-1 major genotype	Drug resistance category	Drug resistance site	Antiviral drugs
1	2020	Homosexual transmission	CRF01_AE	NNRTIs	G190A	L: RPV; I: EFV; H: NVP
2	2021	Heterosexual transmission	CRF01_AE	NNRTIs	E138A	L: RPV
3	2021	Homosexual transmission	CRF55_01B	NNRTIs	E138G, V179E	L: EFV, ETR, NVP, RPV
4	2021	Homosexual transmission	B+CRF01_AE	NNRTIs	E138G, V179E	L: EFV, ETR, NVP, RPV
5	2021	Heterosexual transmission	CRF07_BC	NNRTIs	V106M, Y188D	H: EFV, NVP
6	2022	Heterosexual transmission	CRF01_AE	NNRTIs	V179D	L: RPV; I: EFV, NVP
7	2022	Homosexual transmission	CRF01_AE	NNRTIs	K103N	H: EFV, NVP
8	2022	Heterosexual transmission	CRF01_AE	NNRTIs	V106I, Y181C	I: EFV, ETR; H: NVP, RPV
9	2022	Heterosexual transmission	CRF01_AE	NNRTIs	Y181C	I: EFV, ETR, RPV; H: NVP
10	2022	Homosexual transmission	CRF07_BC	NNRTIs	E138G, V179E	L: EFV, ETR, NVP, RPV
11	2021	Heterosexual transmission	CRF07_BC	NNRTIs	V179D	L: RPV; I: EFV, NVP
				NRTIs	M41L, M184V	L: ABC; H: FTC, 3TC
12	2022	Homosexual transmission	CRF07_BC	NRTIs	M184V	L: ABC; H: FTC, 3TC
13	2022	Homosexual transmission	B+C	NRTIs	M41L, K65R, K70T	I: FTC, 3TC; H: ABC, TDF
14	2022	Heterosexual transmission	CRF07_BC	NRTIs	M184V	L: ABC; H: FTC, 3TC

L: low-level resistance; I: intermediate resistance; H: high-level resistance; PI: protease inhibitor; NNRTIs: non-nucleoside reverse transcriptase inhibitors; NRTIs: nucleoside reverse transcriptase inhibitors; RPV: rilpivirine; EFV: efavirenz; NVP: nevirapine; ETR: etravirine; ABC: abacavir; FTC: emtricitabine; 3TC: lamivudine; TDF: tenofovir. Case number 11 was found to be resistant to both NNRTIs and NRTIs simultaneously.

3 讨论

本研究发现艾滋病住院初治患者的基因亚型存在多样性和复杂性,CRF07_BC最常见,其次是CRF01_AE;2020–2022年,TDR发生率呈逐年升高趋势,TDR总发生率较高,耐药种类以NNRTIs为主,其次为NRTIs,耐药程度以高度耐药为主。研究提示需加强耐药监测,以制定应对策略、减少耐药传播。

本研究检出10种HIV-1基因亚型,其中3种URFs(15例),5种其他亚型(18例),CRF07_BC(77例)和CRF01_AE(67例),显示了住院初治患者HIV-1基因亚型的多样性和复杂性,这可能与四川人口流动较大有关[6],需进一步进行HIV分子流行病学调查研究以证实。本研究中CRF07_BC占比最高,与广东[7]、湖南[8]、河北[9]、上海[10]等地以CRF01_AE为主的情况不同,我国是HIV-1基因亚型最多样化的国家之一,不同地区、不同人群具有不同的

优势亚型[11]。本研究发现近2年, CRF07_BC占比逐渐超过CRF01_AE, 与本地区早年的研究报道[12-13]不同, 结合相关研究[14-16]结果, 提示主要基因亚型已经发生变化, 这可能与CRF07_BC较CRF01_AE具有更强的传播性有关[17], 但需要更深入地调查和研究。本研究中URFs的比例较前[12]增加, 且URFs在中年人群的占比较高, 提示中年患者感染的HIV毒株可能已经发生变异、重组, URFs的出现会导致新的重组毒株产生并进一步流行扩散[6], 因此需加强对本地区HIV-1基因型的监测, 以便更准确地预防和控制HIV传播、减少新的URFs发生[4]。

本研究中TDR总发生率处于中等耐药水平[18], 略低于北京6.68%[19]、南京7.8%[20]、杭州8.1%[21]的TDR发生率。值得注意的是: 本研究发现住院患者TDR发生率逐年升高, 耐药种类以NNRTIs相关耐药为主, 其次为NRTIs耐药, 主要原因为:①HIV耐药检测受到重视, 更多住院患者启动ART前进行耐药检测; ②近几年我省ART方案仍以2NRTIs+NNRTIs为主[22]; ③NNRTIs较NRTIs耐药屏障低、更容易发生耐药[2]。这与目前中国TDR流行趋势相同[23-24]。此外, 本研究发现1例患者发生NNRTIs和NRTIs双重耐药, 对NVP/EFV中度耐药、FTC/3TC高度耐药, 若使用2NRTIs+NNRTIs的一线方案将导致患者治疗失败。因此建议治疗前进行耐药检测, 根据检测结果使用敏感药物进行ART, 以减少耐药发生。

本研究中NNRTIs突变频率最高的是V179、E138, NRTIs突变频率最高的是M184, 与相关研究[25]结果一致, 但本研究不同之处为半数耐药患者为复合突变, 对多个一线NNRTIs、NRTIs药物发生不同程度耐药, 提示住院初治患者发生HIV耐药情况更复杂。复合突变会增加NNRTIs药物耐药水平, 本研究中有3例患者为V179E、E138G复合突变, 表现为对EFV、依非韦伦(ETR)、NVP、利匹韦林(RPV)低度耐药, 有研究[26]报道V179E、E138G复合突变在CRF55_01B亚型的初治患者中发生率最高, 但本研究这3例患者基因亚型均非CRF555_01B。V179E、E138G作为NNRTIs常见的突变位点, 虽然未导致耐药水平显著升高, 但这种复合突变对NNRTIs药物的敏感性、对抗病毒治疗效果的影响及与基因亚型的关系值得进一步研究。

本研究存在一定局限: 为单中心调查, 样本量相对较小, 可能存在抽样偏差, CRF07_BC和CRF01_AE差异不大, URFs和其他亚型占比较小, 无法进一步分析不同基因亚型在人口学特征、感染途径、传播性耐药等方面的差异; 未检测到PIs及INTIs相关耐药。但通过本研究发现, 本地区艾滋病住院初治患者HIV-1基因亚型复杂、多样, 出现了一定比例的特殊、重组、耐药毒株; TDR发生率较高, 耐药突变位点复杂, 对多个一线ART药物耐药。因此建议加强耐药检测, 优化ART治疗、提高疗效、减少耐药传播。

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作者贡献声明　刘欢霞负责论文构思、数据审编、正式分析、调查研究、研究方法、初稿写作和审读与编辑写作, 何盛华负责论文构思、经费获取、调查研究、研究方法、研究项目管理、提供资源、监督指导和审读与编辑写作, 杨彤彤、蔡琳和程殿霞负责提供资源。所有作者已经同意将文章提交给本刊, 且对将要发表的版本进行最终定稿, 并同意对工作的所有方面负责。

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参　考　文　献

[1] PHILLIPS A N, STOVER J, CAMBIANO V, *et al*. Impact of HIV drug resistance on HIV/AIDS-associated mortality, new infections, and antiretroviral therapy program costs in sub-Saharan Africa. J Infect Dis, 2017, 215(9): 1362–1365. doi: 10.1093/infdis/jix089.

[2] World Health Organization. HIV drug resistance report 2021. (2021-11-24) [2023-10-25]. https://www.who.int/publications/i/item/9789240038608.

[3] XU Y, SHI H, DONG X, *et al*. Transmitted drug resistance and transmission clusters among ART-naïve HIV-1-infected individuals from 2019 to 2021 in Nanjing, China. Front Public Health, 2023, 11: 1179568. doi: 10.3389/fpubh.2023.1179568.

[4] LIUX, WANG D, HU J, *et al*. Changes in HIV-1 subtypes/sub-subtypes, and transmitted drug resistance among art-naïve HIV-infected individuals - China, 2004-2022. China CDC Wkly, 2023, 5(30): 664–671. doi: 10.46234/ccdcw2023.129.

[5] 中华医学会感染病学分会艾滋病丙肝学组, 中国疾病预防与控制中心. 中国艾滋病诊疗指南(2018版). 中国艾滋病性病, 2018, 24(12): 1266–1282. doi: 10.13419/j.cnki.aids.2018.12.26.
AIDS and Hepatitis C Group of Infectious Diseases Branch of Chinese Medical Association, China Center for Disease Control and Prevention. Guidelines for AIDS diagnosis and treatment in China (2018 edition). Chin J AIDS Std, 2018, 24(12): 1266–1282. doi: 10.13419/j.cnki.aids.2018.12.26.

[6] ZHOU C, LIANG S, LI Y, *et al*. Characterization of HIV-1 molecular epidemiology and transmitted drug-resistance in newly diagnosed HIV-infected patients in Sichuan, China. BMC Infect Dis, 2022, 22(1): 602. doi:

10.1186/s12879-022-07576-z.

[7] ZHOU P P, YU G, KUANG Y Q, *et al*. Rapid and complicated HIV genotype expansion among high-risk groups in Guangdong Province, China. BMC Infect Dis, 2019, 19(1): 185. doi: 10.1186/s12879-019-3788-7.

[8] 曹旭健, 曹静, 祁慧, 等. 湖南省HIV-1感染者原发性耐药现况调查. 中国感染控制杂志, 2023, 22(4): 451–456. doi: 10.12138/j.issn.1671-9638.20233379.
CAO X J, CAO J, QI H, *et al*. Primary drug resistance in HIV-1 infected individuals in Hunan Province. Chin J Infect Control, 2023, 22(4): 451–456. doi: 10.12138/j.issn.1671-9638.20233379.

[9] 路新利, 王莹莹, 安宁, 等. 2015-2019年河北省HIV-1新发感染因素与基因亚型分析. 中国皮肤性病学杂志, 2023, 37(7): 815–822. doi: 10.13735/j.cjdv.1001-7089.202212115.
WANG X L, WANG Y Y, AN N, *et al*. Analyses of HIV-1 recent infection factor and gene subtypes in Hebei Province from 2015 to 2019, China. Chin J Dermatovenereol, 2023, 37(7): 815–822. doi: 10.13735/j.cjdv.1001-7089.202212115.

[10] ZHANG M, MA Y, WANG Z, *et al*. Prevalence and transmission of pretreatment drug resistance in people living with HIV-1 in Shanghai China, 2017-2021. Virulence, 2024, 15(1): 2373105. doi: 10.1080/21505594.2024.2373105.

[11] 吴楠楠, 殷玥琪, 袁瑞, 等. 我国HIV亚型与耐药性Meta分析. 中华流行病学杂志, 2016, 37(11): 1546–1554. doi: 10.3760/cma.j.issn.0254-6450.2016.11.022.
WU N N, YIN Y Q, YUAN R, *et al*. HIV genetic subtypes and HIV drug resistance in chian: a meta-analysis. Chin J Epidemiol, 2016, 37(11): 1546–1554. doi: 10.3760/cma.j.issn.0254-6450.2016.11.022.

[12] 刘欢霞, 何盛华, 周锐峰, 等. 四川地区HIV/AIDS患者基因亚型及传播性耐药现状研究. 四川大学学报(医学版), 2022, 53(5): 851–856. doi: 10.12182/20220960206.
LIU H X, HE S H, ZHOU R F, *et al*. Genetic subtypes and status of transmitted drug resistance of HIV/AIDS patients in Sichuan. J Sichuan Univ (Med Sci), 2022, 53(5): 851–856. doi: 10.12182/20220960206.

[13] 袁丹, 苏玲, 刘红露, 等. 四川省CRF01_AE和CRF07_BC亚型HIV-1毒株耐药性分析. 中华预防医学杂志, 2015, 49(10): 901–906. doi: 10.3760/cma.j.issn.0253-9624.2015.10.013.
YUAN D, SU L, LIU H L, *et al*. Drug-resistance characteristics of CRF01_AE and CRF07_BC subtypes of HIV-1 strains in Sichuan province. Chin J Prev Med, 2015, 49(10): 901–906. doi: 10.3760/cma.j.issn.0253-9624.2015.10.013.

[14] CAO B, WU C, LIU M, *et al*. Molecular transmission network and drug resistance in treatment-naive HIV-1-infected patients in the Liangshan District, China. AIDS Res Hum Retrovir, 2024, 40(8): 489-495. doi: 10.1089/aid.2024.0016.

[15] HAO J, ZHENG S, GAN M, *et al*. Changing proportions of HIV-1 subtypes and transmitted drug resistance among newly diagnosed HIV/AIDS individuals - China, 2015 and 2018. China CDC Wkly, 2021, 3(53): 1133–1138. doi: 10.46234/ccdcw2021.251.

[16] CHEN H, HAO J, HU J, *et al*. Pretreatment HIV drug resistance and the molecular transmission network among HIV-positive individuals in China in 2022: multicenter observational study. JMIR Public Health Surveill, 2023, 9: e50894. doi: 10.2196/50894.

[17] CHENG Z, YAN H, LI Q, *et al*. Enhanced transmissibility and decreased virulence of HIV-1 CRF07_BC may explain its rapid expansion in China. Microbiol Spectr, 2022, 10(4): e0014622. doi: 10.1128/spectrum.00146-22.

[18] World Health Organization. WHO global strategy for the surveillance and monitoring of HIV drug resistance 2012. (2012-11-01) [2023-10-25]. https://www.who.int/publications-detail-redirect/978-92-4-150476-8.

[19] LI R, SONG C, CHEN D, *et al*. Prevalence of transmitted drug resistance among ART-naïve HIV-infected individuals, Beijing, 2015-2018. J Glob Antimicrob Resist, 2022, 28: 241–248. doi: 10.1016/j.jgar.2022.01.017.

[20] SU Y, QI M, ZHING M, *et al*. Prevalence of HIV transmitted drug resistance in Nanjing from 2018 to 2021. Infect Drug Resist, 2023, 16: 735–745. doi: 10.2147/IDR.S391296.

[21] 叶灵, 许珂, 张兴亮, 等. 杭州市2020—2022年新报告HIV/AIDS人群病毒基因亚型及治疗前耐药分析. 中华微生物学和免疫学杂志, 2023, 43(7): 541–546. doi: 10.3760/cma.j.cn112309-20230330-00077.
YE L, XU K, ZHANG X L, *et al*. Analysis of HIV-1 subtypes and pretreatment drug resistance in newly reported HIV/ AIDS cases in Hangzhou, 2020-2022. Chin J Microbiol Immunol, 2023, 43(7): 541–546. doi: 10.3760/cma.j.cn112309-20230330-00077.

[22] ZHOU C, KANG R, LIANG S, *et al*. Risk factors of drug resistance and the potential risk of HIV-1 transmission of patients with ART virological failure: a population-based study in Sichuan, China. Infect Drug Resist, 2021, 14: 5219–5233. doi: 10.2147/IDR.S334598.

[23] 郭春香, 张洋, 张珂, 等. 中国未治疗的HIV感染者原发耐药情况的Meta分析. 精准医学杂志, 2022, 37(4): 360–364. doi: 10.13362/j.jpmed.202204016.
GUO C X, ZHANG Y, ZHANG K, *et al*. Primary drug resistance in treatment-naive individualswith HIV infection in China--a meta-analysis. J Precis Med, 2022, 37(4): 360–364. doi: 10.13362/j.jpmed.202204016.

[24] XU X, LUO L, SONG C, *et al*. Survey of pretreatment HIV drug resistance and the genetic transmission networks among HIV-positive individuals in southwestern China, 2014-2020. BMC Infect Dis, 2021, 21(1): 1153. doi: 10.1186/s12879-021-06847-5.

[25] 孙卓群, 于凤婷, 陈美玲, 等. 2019-2020年地坛医院HIV-1感染者治疗前耐药及影响因素. 中国艾滋病性病, 2021, 27(11): 1212–1217. doi: 10.13419/j.cnki.aids.2021.11.05.
SUN Z Q, YU F T, CHEN M L, *et al*. Analysis on the prevalence and influencing factors of pretreatment HIV drug resistance among adults at Ditan Hospital in Beijing (2019-2020). Chin J AIDS Std, 2021, 27(11): 1212–1217. doi: 10.13419/j.cnki.aids.2021.11.05.

[26] LIU Y, LI H, WANG X, *et al*. Natural presence of V179E and rising prevalence of E138G in HIV-1 reverse transcriptase in CRF55_01B viruses. Infect Genet Evol, 2020, 77: 104098. doi: 10.1016/j.meegid.2019.104098.

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