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Epidemiology and spatial distribution of people diagnosed with HIV between 1997 and 2020 in Kerman, Iran

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Abstract

Objective: This study described the epidemiology and geographical distribution of people diagnosed with HIV in Kerman, Iran, between 1997 and 2020.

Methods: We used case-based HIV surveillance data of all people diagnosed with HIV in Kerman between 1997 and 2020. We compared the age, gender, modes of transmission and spatial distribution of newly diagnosed HIV-infected people in three time periods (1997-2004, 2005-2012, and 2013-2020). The χ^2 test for trend, one-sample t-test and Kruskal–Wallis H test were used to compare the differences between the three time periods. We also used ArcGIS to map both HIV services and people living with HIV (PLWH) in 2020. The nearest neighbour index (NNI) and kernel density were used to identify the spatial distribution of people living with HIV.

Results: A total of 459 (27.5% women) people were diagnosed with HIV during 1997-2020. The proportion of women (9.3% in 1997-2004 and 48.3% in 2013-2020, $P < 0.001$), HIV infection through sexual contacts (11.6% in 1997-2004 and 50.3% in 2013-2020, $P < 0.001$), HIV infection under the age of 5 years (0.8% in 1997-2004 and 5.4% in 2013-2020, $P = 0.01$) and mean age at

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HM contributed to study design, literature review, data cleaning, data analysis and preparation of early drafts of the paper. AM contributed to study design, analysis interpretation and critical review of the early draft of the manuscript. MB contributed to the study design and preparation of early drafts of the paper. ER contributed to data extraction. SE contributed to study design and analysis interpretation. HSH managed the implementation of the study and contributed to study design and preparation of early drafts of the paper. All authors contributed to the writing of the manuscript and approved the final version.

Conflict of interest: Ebrahim Ranjbar is responsible for Kerman VCT.

diagnosis among men (34.9 in 1997-2004 and 39.8 years in 2013-2020, $P = 0.004$) significantly increased over time. 36.2% of diagnosed cases had CD4 counts under 200 10ˆ6/L between 2013 and 2020, with no significant improvement over time. Most newly diagnosed cases of HIV were from the eastern parts of the city. The clusters of PLWH in 2020 matched with the locations of HIV services.

Conclusion: We observed important changes in HIV epidemiology regarding gender, modes of transmission, number of paediatric cases and density maps over time in Kerman. These changes should be considered for precise targeting of HIV prevention and treatment programmes.

Keywords

Epidemiology; Temporal analysis; Human immunodeficiency virus; Iran

INTRODUCTION

The HIV epidemic in Iran is concentrated among key populations, including men who have sex with men (MSM) (7.0% in a meta-analysis study),[1] people who inject drugs (PWID) (15.2% in 2010, 10.9% in 2014 and 3.6% in 2020)[2-4] and partners of PWID (2.8% in 2010),[5] female sex workers (FSWs) (4.5% in 2010 and 2.1% in 2015)[6 7] and prisoners (1.2% in 2014).[8] The prevalence of HIV is low among the general population (0.15%),[9] blood donors (three per 100,000 donations from 2003 to 2017)[10] and pregnant women (0.04%).[11]

The Joint United Nations Programme on HIV/AIDS (UNAIDS) estimated 59,314 people living with HIV (PLWH) in Iran in 2019, of whom only 22,054 (37.2%) were diagnosed and reported to the National HIV Case-Based Surveillance.[12] Among the diagnosed cases, 67% (25% of estimated cases) were under antiretroviral treatment, and 85% of those under antiretroviral treatment (11% of estimated cases) had viral load suppression. The main gap in the national HIV continuum programme in Iran is the low proportion of diagnosis.[12] Among patients who were diagnosed with HIV in Iran from 1967 to 2018, most of them were male (83%), aged between 16 and 40 years old (67.6%) and infected through injection drug use (61.9%).[11]

In different surveys among key populations in Kerman, HIV prevalence was decreased from 6.2% in 2010[13] to 4.7% in 2020[14] among PWID. In FSWs, we found no positive case in two surveys conducted in 2010 and 2015.[1 15] To our knowledge, no survey in Kerman has studied HIV among MSM so far. Analysis of the HIV continuum of care in Kerman showed that, of an estimated 1,113 of PLWH in 2016, 437 (39.3%) were diagnosed, 10.1% were on antiretroviral treatment and 7.3% had viral suppression.[16] Besides this cascade analysis, epidemiological patterns and spatial and temporal changes in HIV epidemiology have not been studied yet; however, this information is critical for precisely targeting HIV programmes in Kerman. This study aimed to assess the trends in HIV epidemiological and spatial patterns in Kerman between 1997 and 2020.

METHODS

Study design and data

We used case-based surveillance data of all people diagnosed with HIV in Kerman between 1997 and 2020. Demographic data, age, gender, residential address, first CD4 cell count at the time of diagnosis, mode of transmission (MOT) and date of diagnosis were extracted from the HIV surveillance database. We divided the study period (1997-2020) into three equal intervals to have a sufficient sample size for the trend analysis.

Study location and environment

Kerman is located in southeast Iran, with a population of around 540,000 individuals.[17] One HIV voluntary counselling and testing (VCT) centre is responsible for providing care to all people diagnosed with HIV in the city. The VCT is the referral centre for all people who test positive (or reactive) for HIV at any health facility, DIC (drop-in centre), blood transmission organization or laboratory in Kerman and small neighbouring towns. The VCT centre collects and sends blood samples for confirmatory HIV diagnosis to a central public health laboratory in Kerman for any new referral case. After confirmation, the VCT staff will submit data to the electronic portal of the National HIV Surveillance. Kerman University of Medical Sciences supervises the VCT and central public health laboratory.

Spatial data analysis

We used Google Earth to georeference the addresses of the blocks where the people diagnosed with HIV lived (converting the address to a position on the surface of the map).[18] The nearest neighbour index (NNI) was used to identify if the distribution of diagnosed HIV cases was either random or clustered. The NNI was calculated as the observed average distance (D_O) divided by the expected average distance (D_E) (Formula 1). In this formula, the observed average distance is calculated as measuring the distance between each case and its nearest neighbour's case; then, it averages all these nearest neighbour distances. The expected average distance is based on a hypothetical random distribution with the same number of cases covering the same total area. The NNI ranged from 0 to 2.15. If the NNI is less than one, the distribution of cases was considered a cluster. If the index is greater than one, the trend is toward dispersion, and if the index is one, the distribution of cases is considered random.[19] We calculated 95% uncertainty intervals (UI) for the NNI using the bootstrap method by drawing 1000 samples. We produced density maps over the study periods using the kernel density method.[20] ArcGIS version 10 (Esri, New York, NY, USA) was used for spatial data analysis.

Formula 1:
Calculation of the nearest neighbor index (NNI)

$$\mathrm{NNI} = \frac{D_O}{D_E}$$
$$D_O = Observed\ mean\ distance\ between\ each\ case\ and\ its\ nearest\ neighbor$$
$$D_E = Expected\ mean\ distance\ for\ the\ cases\ given\ in\ the\ random\ pattern$$

Epidemiological data analysis

For continuous variables (e.g., age and CD4 count), mean, standard deviation (SD), median and interquartile range (IQR) were reported, and for categorical variables (e.g., age groups, sex, MOT and CD4 count groups), frequencies and percentages were reported. For the trend analysis of categorical variables (including sex, MOT, levels of first CD4 counts and age groups) over the three periods, we used the chi-square and Fisher exact tests. The Kruskal–Wallis H test was used for comparing the distribution of CD4 counts between the three periods. Stata version 17 was used for epidemiological data analysis.

Ethical consideration

We received the deidentified data from the HIV program. The spatial data only included the coordinates of the blocks instead of the actual location of the households of the people living with HIV. All data were secured and stored in an encrypted password-protected computer which were only accessible to one of our team members who did the analysis. The study protocol and procedures were reviewed and approved by the Research Ethics Committee of Kerman University of Medical Science (Ethics code: IR.KMU.REC.1399.618).

RESULTS

Between September 1997 and December 2020, 459 HIV-positive cases were diagnosed in VCT centres in Kerman. Of whom, 105 cases had a residential address outside of Kerman and 41 cases were homeless. As a result, they were excluded from the spatial analysis. Therefore, 313 cases (68.2% of all diagnosed cases) remained in the spatial analysis. Analysis of epidemiological patterns was performed on all 459 cases.

Epidemiological pattern

The mean (SD) age of all registered cases was 36.1 (9.0) years, 36.7 (8.1) years in men and 34.4 (11.0) years in women. The mean age was not significantly different between the three periods ($P = 0.07$). However, the mean age of HIV-positive males increased significantly from 34.9 years in 1997-2004 to 36.6 in 2005-2012 to 39.8 years in 2013-2020 ($P = 0.004$; Table 1).

Most of the 459 HIV cases were male (n = 333, 72.5%). The proportion of female cases significantly increased over time from 9.3% in 1997-2004 to 23.5% in 2005-2012 to 48.3% in 2013-2020 ($P < 0.001$). The proportion of HIV-infected children under 5 years of age increased from 0.8% in 1997-2004 to 5.4% in 2013-2020 ($P = 0.01$). Unsafe injection (48.4%) and unprotected sex (30.3%) were the main MOT overall. The proportion of sexual contact as the MOT significantly increased from 11.6% in 1997-2004 to 27.3% in 2005-2012 to 50.3% in 2013-2020 ($P < 0.001$). For females, the main MOT was sexual contact in all three time periods. For males, the main MOT in the first two time periods was unsafe injection (70.9% in 1997-2004 and 77.1% in 2005-2012), which changed to sexual contact during the third time period (39.5%). Overall, the median (IQR) of the CD4 count at diagnosis was 260 (101-484) x 10ˆ6/L. In 41.8% of cases, the CD4 count at diagnosis was under 200 × 10ˆ6/L. The median CD4 count at diagnosis and the proportion of patients with a CD4 count under 200 × 10ˆ6/L did not change significantly over time (Table 1).

Spatial pattern

The NNI for newly diagnosed cases was 0.46 (95% UI: 0.31-0.62) in 1997-2004, 0.36 (95% UI: 0.28-0.47) in 2005-2012 and 0.39 (0.95% UI: 0.28-0.51) in 2013-2020, which was clearly less than one (P< 0.001; i.e., an indication of a clustered pattern).[19] The result of the kernel density estimation showed that the distribution of newly diagnosed cases of HIV was more concentrated in the eastern parts of the city (Figure 1). The density map of residents with HIV infection had the highest density (6.01-9 cases per km^2) in the northern and southern edges of the city in 2005-2012.

The NNI for PLWH in 2020 was 0.40 (95% UI: 0.29-0.53), suggesting a high cluster pattern. The HIV density map in 2020 (Figure 2) shows a high density in areas corresponding to locations of VCT centres, DICs and two mobile clinics.

DISCUSSION

We observed important changes in the HIV epidemiology regarding gender, MOT, number of paediatric patients and density maps over time in Kerman from 1997 to the end of 2020. Over time, more HIV was diagnosed among women, through sexual contacts and in children under 5 years of age than in the past. The average age at diagnosis among male individuals also increased over time. We found that more than one in three patients had a late diagnosis (CD4 count under 200 × 10ˆ6/L), which has not been improved over time. In the spatial analysis, we found a cluster of HIV cases in the eastern neighbourhoods of the city; the density map also showed there was a shift over time, with the highest density in the northern and southern edges of the city in 2005-2012. The HIV clusters of PLWH in 2020 were matched with the locations of fixed and mobile HIV services.

We found that the proportion of women diagnosed with HIV increased cautiously over time. In 1997-2004, less than 10% of the registered cases were women; however, around 50% of the registered cases were women in 2013-2020. We also found the same pattern for sexual transmission over time. This changing pattern from male to female and unsafe injection to sexual contact led to an increase in the number of reported cases due to mother to child transmission (from one case in 1997-2004 to eight cases in 2013-2020). This pattern is similar to the pattern observed in the national information[21] and in some other cities in Iran, such as Kermanshah (for gender)[22] and Yazd (for MOT).[23] These changes could be explained by the overall change in sexual behaviours in the country over the last two decades. Having more than two clients among FSWs in the last month increased from 46.6% in 2010 to 63.4% in 2015;[7] extramarital sex among female youth increased from 8% in 2008[24] to more than 13% in 2018;[25] and injection drug use among FSWs increased from 14% in 2010[26] to 25% in 2015.[27] However, there was no significant increase in condom use among FSWs (condom use in the last month was 26.1% in 2010 and 26.3% in 2015).[7] Moreover, some parts of the changing pattern in MOT can be explained by increasing HIV infections among spouses of HIV-infected people in Kerman. A study showed that people infected through HIV-infected spouses increased from 8.8% in 2007 to 19% in 2016.[16] Different population size studies in Kerman showed around 12.0% of the males reported extramarital sex, 7.0% of them had sex with FSWs and 2.5% of them had at least one sexual contact with other males.[28] Around 1.2% of the city population were PWID, and around

1.0% of the females aged 15-49 were FSWs.[29] Condom use in the last sexual contact with paying and non-paying partners was 17% and 22%, respectively.[30]

Reducing the number of cases infected through injection is a great public health achievement. Iran has expanded hard drug reduction programmes over the past decades. The number of methadone maintenance treatment (MMT) centres increased from 5,893 in 2014 to more than 8,000 centres in 2019. The number of drug users who have received MMT also increased from 476,0000 individuals in 2011[21] to more than 750,000 individuals in 2019.[31] Moreover, shared injections among PWID decreased from 36.9% in the last month in 2010[2] to 4.1% in the last three months in 2020.[4]

We also found that more than three-fourths of diagnosed cases had a CD4 count ≤ 500 × 10ˆ6/L at the time of diagnosis, and more than 40% had a CD4 count < 200 × 10ˆ6/L at diagnosis. These figures were almost similar over time, which shows a continuous problem of late diagnosis of the majority of the infected cases. Several interventions have been implemented in Iran to improve HIV testing in recent years. For example, HIV rapid tests have been implemented as a routine part of counselling services in health services and harm reduction settings.[32] The HIV testing protocol was also updated based on WHO guidelines that suggested health care providers offer HIV testing as part of routine medical care to all people attending their facilities. Also, mobile HIV testing clinics were developed to increase access to HIV testing for high-risk populations with limited access to healthcare facilities.[33] Due to these interventions, HIV testing uptake in the last 12 months increased from 27% in 2010 to 70.4% in 2015 among FSWs,[33] and from 24% in 2010 to 71% in 2019 among PWID.[31] Despite the overall increase in HIV testing, early detection rates have not been improved significantly.[31] It is not clear how many of those who tested for HIV continue to test themselves frequently as long as they are at risk or belong to a high-risk group. Repeated HIV testing was recently (in 2021) added to the national HIV testing guideline, which recommended members of high-risk groups (including sexual partners of PLWH, PWID and their sexual partners, FSWs, MSM and prisoners) to be tested for HIV every 3 months. If appropriately implemented, this strategy is expected to increase the chance of a diagnosis of HIV at the early stages of infection. The proportion of high-risk populations who test for HIV frequently needs to be monitored by surveys and surveillance information.

We also found that the diagnosed cases were clustered in the eastern neighbourhoods of the city. A study conducted in another city in Iran (Kermanshah) also showed spatial clusters of HIV cases.[22] The higher density of HIV diagnosed cases in the eastern parts of the city can be explained by a higher concentration of population, lower socioeconomic status and higher rates of high-risk behaviours in these neighbourhoods.[34 35] The density of the diagnosed cases has also shifted over time, with the highest density in the northern and southern edges of the city in 2005-2012. Shifting of the highest density to the northern and southern edges of the city can be explained by developing a new transmission cluster in these neighbourhoods. This spatial clustering of the cases could help healthcare providers to focus on these clusters for better case finding, identifying high-risk groups and directing preventive interventions based on high-risk groups in these neighbourhoods. We also found fixed and mobile health services matched these clusters in 2020. There is one VCT centre in the city, which has been established in the centre of the city, and it seems the location of the VCT centre, in terms of access to all hotspots, is reasonable. DICs were also close to the hotspots and approximately covered all areas with a higher density of HIV-infected patients; the overlap between these DICs is low. DICs provide harm reduction services to the high-risk populations in place or outreach services.

We acknowledge four main limitations of our study. First, we used HIV registry data in our analysis, which had missed data on some of the key variables (CD4 at diagnosis was missing in almost half of cases, MOT was missing in one-fifth of cases and residential address was missing in about 10% of all cases). Although missing data has been improved over time, we could not investigate the pattern and reasons for the missing data. Second, we could not differentiate the different ways of sexual contact (FSWs, MSM, or sexual partners of high-risk groups) as case-based surveillance in Iran did not differentiate them. Third, since there was no specific address assigned to homeless people diagnosed with HIV, we excluded around 9% of the registered cases from the spatial analysis. Potentially, this can affect the geographical distribution of the total registered cases. However, an unpublished study in Kerman[35] showed the distribution of gathering homeless people matched to the same locations for HIV cases. So, we think excluding homeless people from the spatial analysis may not affect the geographical distribution. Finally, the density map of HIV patients based on residential address may not necessarily match with the risk maps where the sexual or injection risk is taking place.

CONCLUSION

Our epidemiological and spatial analyses showed significant changes in the HIV epidemiology regarding gender, MOT, number of paediatric cases and density maps over time. This information can help precisely target HIV prevention, testing, treatment and outreach programmes in the city.

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Key Messages

- Over time, more HIV infection diagnosed among women, through sexual contacts and in children under 5 over time than in the past.
- More than one third of HIV cases had CD4 count <200 × 10ˆ6/L at diagnosis which has not improved over time.
- Most newly diagnosed cases of HIV were from the eastern parts of the city.
- The clusters of people living with HIV in 2020 matched with the locations of HIV services.

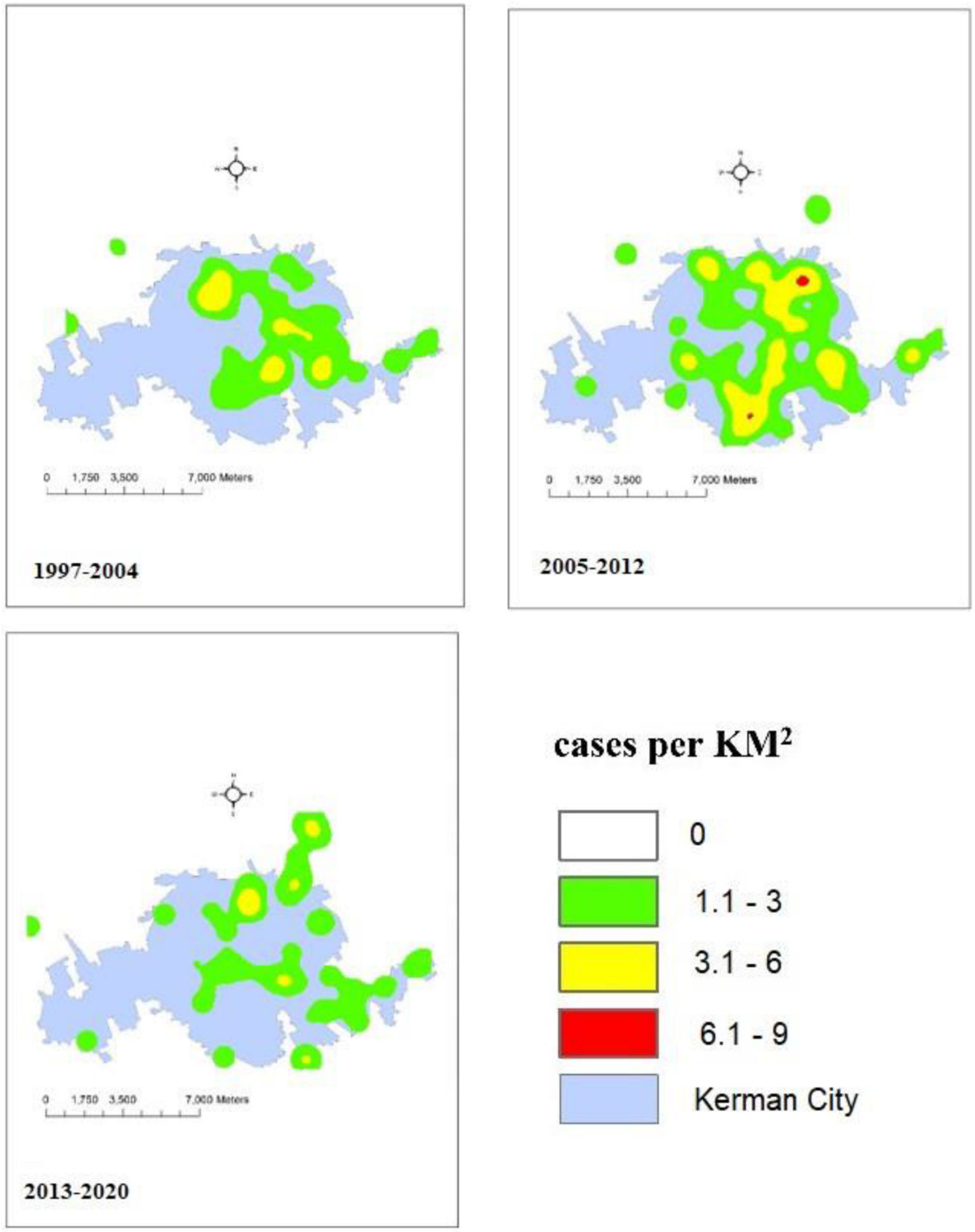

Figure 1:
spatial distribution of people diagnosed with HIV over the study period (1997-2020) in Kerman city

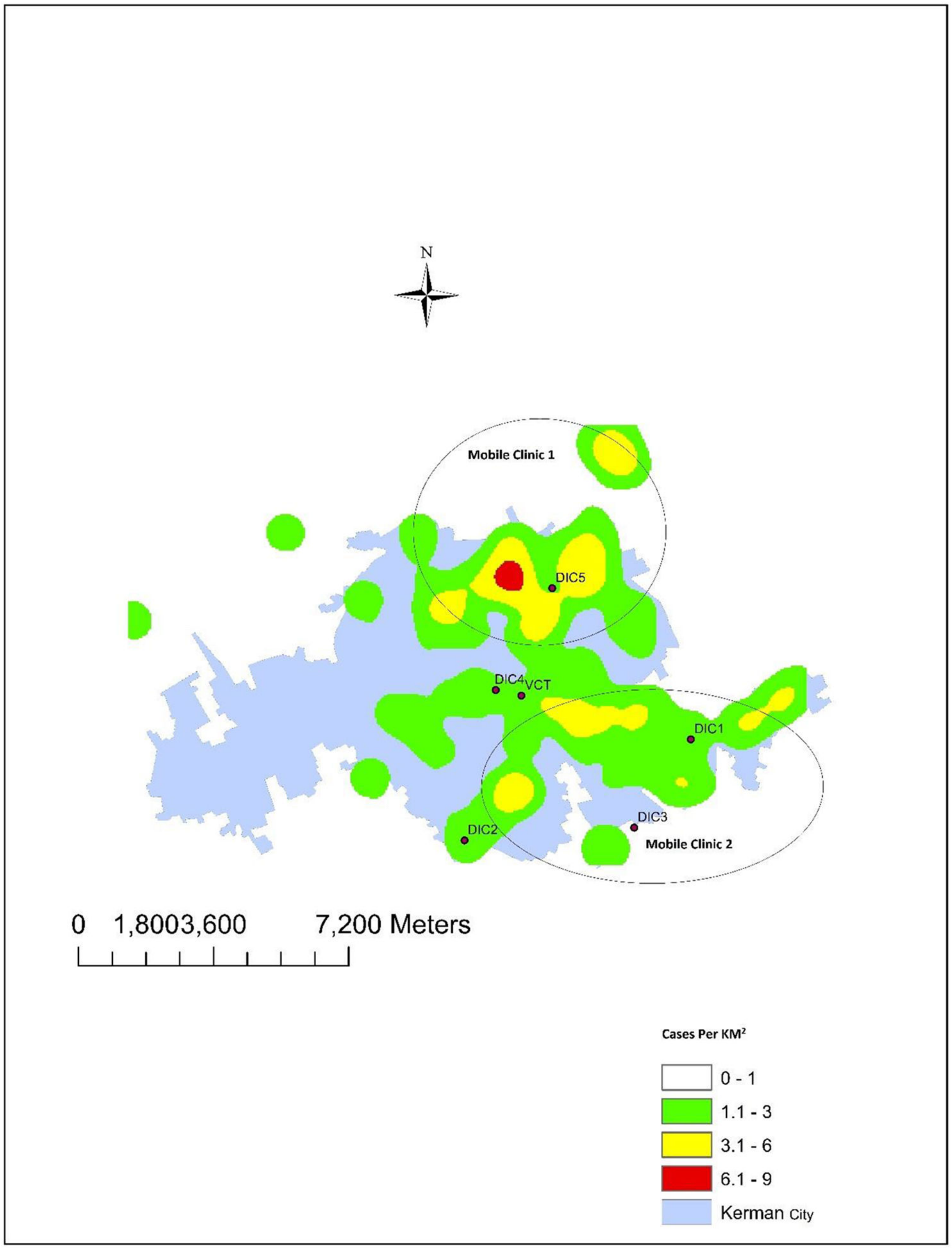

Figure 2:
spatial distribution of people living with HIV in Kerman city in 2020.

Table 1:

Epidemiological characteristics of newly diagnosed cases during three periods in Kerman city (1997-2020).

Ordinal/Nominal Variables	**Total (N=459) n (%)**	**1997-2004 (N=129) n (%)**	**2005-2012 (N= 183) n (%)**	**2013-2020 (N=147) n (%)**	**P-value**
Age Groups (Years)					
≤ 5	10 (2.2)	1 (0.8)	1 (0.5)	8 (5.4)	0.01
5 - 14	3 (0.7)	0 (0.0)	2 (1.1)	1 (0.7)	
15 - 24	24 (5.2)	10 (7.8)	6 (3.3)	8 (5.4)	
25 - 34	157 (34.2)	50 (38.8)	75 (41.0)	32 (21.8)	
35 - 44	196 (42.7)	59 (45.7)	70 (38.3)	67 (45.6)	
≥ 45	69 (15.0)	9 (7.0)	29 (15.8)	31 (21.1)	
MOT-Total cases					
unsafe injection	222 (48.4)	84 (65.1)	111 (60.7)	27 (18.4)	<0.001
sexual contact	139 (30.3)	15 (11.6)	50 (27.3)	74 (50.3)	
Mother to child	12 (2.6)	1 (0.8)	3 (1.6)	8 (5.4)	
Unknown	86 (18.7)	29 (22.5)	19 (10.4)	38 (25.9)	
MOT-Female cases					
unsafe injection	5 (4.0)	1 (8.3)	3 (7.0)	1 (1.4)	<0.001
sexual contact	90 (71.4)	9 (75.0)	37 (86.0)	44 (62.0)	
Mother to child	6 (4.8)	1 (8.3)	2 (4.7)	3 (4.2)	
Unknown	25 (19.8)	1 (8.3)	1 (2.3)	23 (32.4)	
MOT-Male cases					
unsafe injection	217 (65.2)	83 (70.9)	108 (77.1)	26 (34.2)	< 0.001
sexual contact	49 (14.7)	6 (5.1)	13 (9.3)	30 (39.5)	
Mother to child	6 (1.8)	0 (0.0)	1 (0.7)	5 (6.6)	
Unknown	61 (18.3)	28 (23.9)	18 (12.9)	15 (19.7)	
Cases with available CD4 count at diagnosis	278 (50.6)	28 (21.7)	112 (61.2)	138 (93.9)	
CD4 cell count at diagnosis (Cell × 10ˆ6/L)					
<200	116 (41.8)	12 (42.9)	54 (48.2)	50 (36.2)	0.23
200-350	59 (21.2)	4 (14.3)	20 (17.9)	35 (25.4)	
350-500	37 (13.3)	7 (25.0)	12 (10.7)	18 (13.0)	
>500	66 (23.7)	5 (17.8)	26 (23.2)	35 (25.4)	
Gender					
Male	333 (72.5)	117 (90.7)	140 (76.5)	76 (51.7)	<0.001
Female	126 (27.5)	12 (9.3)	43 (23.5)	71 (48.3)	
Continuous Variables	**Total (N=459) Mean (SD)**	**1997-2004 Mean (SD)**	**2005-2012 Mean (SD)**	**2013-2020 Mean (SD)**	**P-value**
Age Mean (SD) (Year)					
Female	34.4 (11.0)	30.1 (11.3)	35.7 (10.8)	34.5 (11.1)	0.37
Male	36.7 (8.1)	34.9 (6.3)	36.6 (8.0)	39.8 (10.1)	0.004
Total	36.1 (9.0)	34.3 (7.1)	36.4 (8.7)	37.4 (10.8)	0.07

CD4 (cells × 10ˆ6/L) (Median (IQR))	260 (101-484)	250 (78-438)	248.5 (108-480)	281 (109-514)	0.53

MOT, Modes of transmission