The value and implementation of routine ophthalmic examination in the era of HAART

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ABSTRACT

Background: The high prevalence of ocular manifestations (OMs) in patients with human immunodeficiency virus (HIV) infection and chronic diseases such as diabetes has become a global health issue. However, there is still a lack of an appropriate ophthalmic diagnostic procedure for the early detection of OMs in this population, leading to the risk of an irreversible visual impairment that substantially affects the quality of life of these patients.

Methods: The Guangzhou HIV Infection Study was a retrospective study that enrolled hospitalised HIV-infected patients in Guangzhou between January 2005 and December 2016, period corresponding to the highly active antiretroviral therapy (HAART) era in China. We collected data on OMs, systemic diseases, hospitalisation, and demographic characteristics. We classified the patients into 3 groups according to the ophthalmic examination mode they underwent: the non-ophthalmologist examination group (patients hospitalised in 2005/2011 who were only treated by infectious disease physicians), the on-demand ophthalmic examination group (patients hospitalised in 2012/2013 who were referred for a consultation with an ophthalmologist), and the routine ophthalmic examination group (patients hospitalised in 2014–2016 who routinely underwent standard ophthalmic examinations). Binary logistic regression models were used to investigate the factors related to OMs.

Findings: A total of 8,743 hospitalised HIV-infected patients were enrolled. The prevalence of detected OMs were 1.5% in the non-ophthalmologist examination group, 1.9% in the on-demand ophthalmic examination group, and 12.8% in the routine ophthalmic examination group. The odds of detection of OMs were highest in the routine ophthalmic examination group (adjusted odds ratio [aOR]=9.24, [95%CI, 6.51–13.12], compared to the non-ophthalmologist examination group). The detection of all types of OMs increased substantially, with keratitis, retinitis and vascular abnormalities increased the most (by 15.8–20.0 times). In the routine examination group, patients who were older than 50 years, males, with medical insurance, and were not resident in Guangzhou, had higher odds to have OMs. Several systemic diseases also increased the odds of OMs, with the highest odds among patients with a cytomegalovirus infection (aOR=5.59, [95%CI, 4.12–7.59]). Patients with retinitis, retinopathy and conjunctivitis had higher odds of having a CD4+ T cell counts less than 200 cells/µL compared to the patients that did not have these referred OMs.

Interpretation: The implementation of a routine ophthalmic examination has improved the odds of OM detection by approximately 9 times and increased the diagnosis rates of all types of OMs. Therefore, we encourage all HIV-infected patients to undergo regular ophthalmic examinations. Patients with OMs, especially retinopathy and retinitis, need to be evaluated for immune function (such as CD4+ T cell counts) and systemic diseases.

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1. Introduction

Human immunodeficiency virus (HIV) infection has become a manageable chronic disease with the universal use of highly active antiretroviral therapy (HAART). Mortality has been significantly reduced, but the resulting prolonged life spans have led to an increase in the number of non-fatal complications [1–5], including ocular manifestations (OMs) that seriously affect the quality of patient life [6–13].

Similar to diabetes, HIV infection can cause various OMs, which have become a global health problem in patients with chronic diseases. Although the OMs prevalence has decreased compared to the pre-HAART era, as many as 48% of HIV-infected patients have been diagnosed with OMs in the HAART era [6,11,14–22]. Early diagnosis of OMs is critical for the timely treatment and determination of the prognosis of HIV infection, as the impaired visual function can decrease productivity [9,17,18,23,24], and increase the cost of treatment [25,26].

However, the diagnosis of OMs in HIV-infected patients is often delayed. Many patients with OMs are not diagnosed until a severe visual impairment has developed [6,8–10,18,27]. Methods to balance medical resources and develop appropriate ophthalmic examination procedures to ensure that patients obtain a timely ophthalmic diagnosis and necessary treatments, have been a problem for patients with HIV infection and many chronic diseases [3,5,28–31].

To explore the appropriate pattern for the early detection of OMs in patients with HIV infection and similar chronic diseases, we conducted the Guangzhou HIV Infection Study, which enrolled hospitalised HIV-infected patients in Guangzhou Eighth People’s Hospital, the designated infectious disease treatment centre for patients diagnosed with HIV infection. We 1) analysed the association of the ophthalmic examination mode with the prevalence of detected OMs, 2) investigated the variation in detected OMs, and 3) analysed the association of demographic characteristics and systemic diseases with the presence of OM. The study provides reliable evidence and suggestions for the management of non-fatal complications in patients with HIV infection and other chronic diseases.

2. Methods

2.1. Study design and participants

The Guangzhou HIV Infection Study was a retrospective study that enrolled HIV-infected patients hospitalised in Guangzhou between Jan 1, 2005, and Dec 31, 2016. All the enrolled inpatients met the HIV diagnostic criteria. They received HAART according to the Chinese guidelines for AIDS diagnosis and treatment [32,33]. All the data was extracted from the Guangzhou Eighth Hospital medical record and the related ophthalmologic consultation records. Because the data was initially checked and recorded by the hospital staff during the admission procedures, there was no missing data. Data on the discharge diagnosis and demographic characteristics were then extracted. The unknown information was initially recorded as ‘unknown’ or ‘other’ and was categorized as “other or unspecified” for analysis.

Patients diagnosed with ophthalmic diseases during hospitalisation, excluding ocular trauma and congenital eye diseases, were defined as patients with OMs. The remaining patients were defined as normal patients. The selected hospitalisation for analysis were 1) the first hospitalisation of normal patients and 2) the first hospitalisation with any OM diagnosis of patients with OMs. Every participant was counted once. Fig. 1 shows the enrolment of patients.

This study followed the tenets of the Declaration of Helsinki and was approved by the Institutional Review Board of Zhongshan Ophthalmic Center (2019KYPJ177), Guangzhou, China. Written consent was waived because many patients were lost to follow-up, and the study did not involve personal identifiers or commercial interests. All patient records and information were anonymised and deidentified before analysis.

2.2. Ophthalmic examination procedure

To compare the influence of the mode of ophthalmic examination, the patients were divided into three groups according to the ophthalmic examination mode they underwent: the non-ophthalmologist examination group (2005–2011), the on-demand ophthalmic examination group (2012–2013) and the routine ophthalmic examination group (2014–2016).

In the non-ophthalmologist examination group (2005–2011), the patients were treated by infectious disease physicians without referral to an ophthalmologist. Due to the lack of ophthalmic equipment and professional eye examination, OMs were diagnosed based on inquiry and previous medical history. In the on-demand ophthalmic examination group (2012–2013), as an ophthalmology department had been established, patients were referred to an ophthalmologist if they had OM-related symptoms. In the routine ophthalmic examination group (2014–2016), the ophthalmic examination was routinely provided at admission. Every hospitalised HIV-infected patient was referred to the ophthalmology department for ophthalmic examinations if the patient’s condition permitted the examination.

In the on-demand ophthalmic examination group (2012–2013) and the routine ophthalmic examination group (2014–2016), the patient who was referred to the ophthalmology department would be offered ophthalmic examinations, including a visual acuity test, a non-contact intraocular pressure test, slit-lamp examination, and fundoscopy, performed by a qualified ophthalmologist. The visual acuity test includes a naked visual acuity test and a best-corrected visual acuity test at a distance of 5 m. If the visual acuity was less than 6/60, the distance would be reduced, and the visual acuity was calculated accordingly. A visual acuity below 1/60 would be recorded as finger counts (FC), hand movements (HM), perceives light (PL) and
unable to perceive light (NPL) accordingly. The slit lamp examination was performed with both diffuse light and slit light to examine the anterior segment before dilation. If the patient does not have a history or risk factor of glaucoma, a dilated funduscopy exam would be performed. Further examinations, such as ultrasound biomicroscopy and optical coherent tomography scans, were also performed if needed. The OM diagnosis was then recorded on the consultation record, which is part of the discharge diagnosis after hospitalisation.

2.3. Classification of discharge diagnosis

The ocular diagnosis was extracted from the discharge diagnosis, and was classified according to the location and the type of the OMs [10]. Cases which were of small numbers or not able to classify were assigned to the “other disorders” category. When regarding the location of lesion, this category includes pterygium, glaucoma, herpes zoster uveitis, endophthalmitis, ophthalmitis, and blindness. When regarding the type of the lesion, this category additionally includes vitreous opacity, retinal detachment and unclassified uveitis.

Systemic diseases with high prevalence rates or significant effects on survival outcomes were also classified to analyse their association with the presence of OM.

2.4. Statistical analysis

When comparing the distributions of characteristics between groups, Student’s t test was used to compare the age as a continuous variable, while the chi-square test was used for other categorical variables, including sex, age group, location of the permanent residence, job classification, payment method, and marital status. Since the number of patients with OMs was small in both the non-ophthalmologist examination group (2005–2011) and the on-demand ophthalmic examination group (2012–2013), and no significant difference in the prevalence of detected OMs was observed between these two groups, the two groups were combined into a non-routine ophthalmic examination group (2005–2013) for the characteristic comparison.

Binary logistic regression was used to assess the association between OMs and potential related factors. All the variables, including ophthalmic examination mode and the other factors (sex, age group, location of the permanent residence, job classification, payment method, marital status, whether diagnosed with a disease, and immunity outcome [whether CD4+ T cell count < 200 cell/μL]), were used as categorical variables in the regression models.

To analyse the association of ophthalmic examination mode with the detection of OM, the odds ratio (OR) of the ophthalmic examination mode was calculated without and with adjustments for age group, sex and other potential confounding factors. These factors include the location of the permanent residence, job classification, payment method, and marital status.

To further analyse the association of these potential confounding factors with the presence of OM, and also to analyse the association of systemic diseases with the presence of OM, the data was restricted to the data from the routine examination group (2014–2016). Because all the hospitalised HIV-infected patients in this group underwent routine ophthalmic examinations, the prevalence of detected OMs could therefore represent the true prevalence of OMs in this period.

Data analysis was performed using STATA version 14.0 (Stata Corp., College Station, TX). All tests were two-sided, and P values less than 0.05 were considered statistically significant.

2.5. Role of funding

The source of funding played no role in the design of the study protocol; the data collection, analysis, and interpretation; the writing of the report; or the decision to submit the manuscript for publication.

3. Results

3.1. Association of ophthalmic examination mode with OM detection

A total of 8,743 hospitalised HIV-infected patients with 15,116 hospitalisation records were enrolled in this study (Fig. 1). 667
patients (7.6%) with 1,580 records had OMs. Despite the overall increase in the number of hospitalised HIV-infected patients, the annual prevalence of detected OMs remained low, ranging between 0.9% and 2.9% before 2013 (Fig. 2). After 2014, the prevalence increased substantially from 7.3% to 17.1%, as ophthalmic examinations became a routine practice in hospitalised HIV-infected patients, the annual prevalence of detected OM sharply increased from 7.3% to 17.1%. Therefore, OMs were detected in 38 (1.5% of 2,494) HIV-infected patients in the non-opthalmologist examination group, 30 (1.9% of 1,578) in the on-demand ophthalmic examination group, and 599 (12.8% of 4,671) in the routine ophthalmic examination group (Table 1). The characteristics of patients were compared in Table 2. The unadjusted odds of detection of OMs were highest in the routine ophthalmic examination group (odds ratio [OR]=9.51, [95%CI, 6.82–13.25], compared to the non-opthalmologist examination group) in model 1 in Table 1.

After adjusting for the demographic characteristics in Table 2, the odds of detection of OR remained the highest in Table 1 (in model 2 that was adjusted for age group and sex, adjusted OR [aOR]=8.93, [95%CI, 6.40–12.45], compared to the non-opthalmologist examination group; in model 3 that was additionally adjusted for more demographic characteristics, aOR=9.24, [95%CI, 6.51–13.12], compared to the non-opthalmologist examination group). However, no significant difference was observed between the non-opthalmologist examination group and the on-demand ophthalmic examination group.

To analyse the association of demographic characteristics with the presence of OMs, we restricted the analysis to the routine ophthalmic examination era (a total of 4,671 patients, Table 3). The results show that females were less likely to develop OMs (aOR = 0.71, [95%CI, 0.56–0.90], compared to males). Patients who paid without health insurance also had lower odds of having OMs (aOR = 0.68, [95%CI, 0.55–0.87], compared to the self-paying patients). Patients of 50-59 years old (aOR = 1.52, [95%CI, 1.14–2.01]) and more than 60 years old (aOR = 1.92, [95%CI, 1.43–2.57]) were more likely to develop OMs, compared to the patients of 30-39 years old. The local patients (patients resident in Guangzhou City) had lower odds of having OMs (aOR = 0.45, [95%CI, 0.35–0.57]), compared to patients not resident in Guangzhou City. Therefore, patients that were older than 50 years old, males, paid with medical insurance, and were not resident in Guangzhou, would have higher odds to have OMs.

3.2. Variation in OMs

Although opportunistic infections had the highest prevalence of detection in both the non-routine ophthalmic examination group and the routine ophthalmic examination group, several differences were noted in the locations and nature of OMs (Fig. 3 and Supplementary Table 1). First, conjunctivitis was detected the most common infection in the non-routine ophthalmic examination group (17 patients [0.4%]), whereas vascular abnormalities (229 patients [4.9%]) and retinitis (181 patients [3.9%]) became the most common in the routine ophthalmic examination group (Fig. 3a). Second, from the non-routine ophthalmic examination period to the routine ophthalmic examination period, the prevalence of all types of detected OMs has increased substantially, with keratitis, retinitis and vascular abnormalities increased the most (by 15.8–20.0 times, Supplementary Table 1). At the same time, the prevalence of diagnosed corneal diseases increased from 0.1% to 1.8% (82 patients), and the prevalence of diagnosed retinal disorders increased from 0.4% (11 patients) and 0.8% (12 patients) to 8.3% (386 patients) (Fig. 3b).
3.3. Association of systemic diseases with any OM

Association of systemic diseases with any OM (adnexa) (Fig. 4b). In contrast, the patients of 30-49 years olds had a 29 or patients older than 50 had a higher prevalence of ocular surface diseases (3.2-7.2%). Cataract was very common (10.5%) in patients with cytomegalovirus infection had the highest odds of OMs (aOR=5.59, [95%CI, 4.12–7.59], compared to the patients without cytomegalovirus infection), followed by three metabolic diseases (electrolyte disturbance [aOR=2.24, [95%CI, 1.74–2.88]], hypoproteinemia [aOR=2.12, [95%CI, 1.29–3.49]], and diabetes [aOR=1.74, [95%CI, 1.14–2.64]], compared to the patients without the referred disease). Patients with diseases of the respiratory system (pulmonary infection), digestive system (liver cysts and enteropathy), and nervous system (encephalopathy) had less high odds of developing OMs compared to the patients without the referred disease. In contrast, patients with marasmus, heart failure, and infection of Pneumocystis carinii had lower odds of having OMs compared to the patients without the referred disease.

Table 4 shows the association between systemic diseases and the presence of OM in HIV-infected patients in the routine ophthalmic examination group. In the multivariate model adjusted for all the diseases in Table 4, patients with cytomegalovirus infection had the highest odds of OMs (aOR=5.59, [95%CI, 4.12–7.59], compared to the patients without cytomegalovirus infection), followed by three metabolic diseases (electrolyte disturbance [aOR=2.24, [95%CI, 1.74–2.88]], hypoproteinemia [aOR=2.12, [95%CI, 1.29–3.49]], and diabetes [aOR=1.74, [95%CI, 1.14–2.64]], compared to the patients without the referred disease). Patients with diseases of the respiratory system (pulmonary infection), digestive system (liver cysts and enteropathy), and nervous system (encephalopathy) had less high odds of developing OMs compared to the patients without the referred disease. In contrast, patients with marasmus, heart failure, and infection of Pneumocystis carinii had lower odds of having OMs compared to the patients without the referred disease.

Table 5 shows the associations between common ocular disorders with immunodeficiency. In the multivariate model adjusted for age group, sex, and all the diseases in Table 5. Patients with retinitis (aOR=3.66, [95%CI, 2.29–5.86]), retinopathy (aOR=2.59, [95%CI,
Fig. 3. Prevalence variation of detected ocular manifestations (OMs) in different ophthalmic examination groups. 2005-2011: non-ophthalmologist examination group. 2012-2013: on-demand ophthalmic examination group. 2014-2016: routine ophthalmic examination group. The number of hospitalised HIV-infected patients in each ophthalmic examination group was used as the denominator (2,494 individuals in 2005-2011, 1,578 individuals in 2012-2013, and 4,671 individuals in 2014-2016). a. The prevalence of all types of detected OMs increased substantially, with keratitis, retinitis and vascular abnormalities increased the most (by 15.8-20.0 times, Supplementary Table 1). b. The prevalence of detected OMs of different locations also increased. Both panel a and b indicate an improved accuracy of the OM diagnosis.

Fig. 4. Prevalence variation of ocular manifestations (OMs) in different age groups in the routine ophthalmic examination group (2014-2016). The number of all the hospitalised HIV-infected patients in each age group in the ophthalmic examination group (2014-2016) was used as the denominator (94 individuals in ‘<20’, 848 individuals in ‘20-29’, 1,248 individuals in ‘30-39’, 1,267 individuals in ‘40-49’, 6,89 individuals in ‘50-59’, 525 individuals in ‘≥60’. a. Opportunistic infection was also the main type of OM in all age groups. b. Ocular surface diseases were more common in patients that were younger than 29 or older than 50, while the patients of 30-49 years old had a higher prevalence of the posterior segment diseases of the eye.
The relationship between ocular manifestations (OMs) and CD4+ T cell counts <200 cells/μL. The logistic regressions were conducted based on 599 patients with OMs in the routine ophthalmic examination group (2014-2016). Whether CD4+ T cell count <200 cells/μL was used as a categorical variable and the outcome of the regression models. Model 1: Logistic regression model that includes age group, sex, and the selected disease. Model 2: Logistic regression model that includes age group, sex, and all the diseases in the table. OR: odds ratio.

| Parameter | Model 1 OR (95%CI) | P | Model 2 OR (95%CI) | P |
|-----------|---------------------|---|---------------------|---|
| Retinopathy | 2.09 (1.25, 3.49) | 0.005 | 2.59 (1.51, 4.44) | 0.001 |
| Retinitis | 2.58 (1.69, 3.94) | <0.001 | 3.66 (2.29, 5.86) | <0.001 |
| Uveitis | 0.72 (0.47, 1.10) | 0.129 | 0.75 (0.47, 1.18) | 0.216 |
| Cataract | 0.38 (0.23, 0.60) | <0.001 | 0.47 (0.28, 0.77) | 0.003 |
| Pterygium | 1.17 (0.61, 2.22) | 0.640 | 1.39 (0.70, 2.73) | 0.347 |
| Keratitis | 1.14 (0.52, 2.47) | 0.747 | 1.46 (0.65, 3.27) | 0.359 |
| Retinal detachment | 0.54 (0.28, 1.04) | 0.065 | 0.51 (0.25, 1.02) | 0.056 |
| Fundus haemorrhage | 0.75 (0.33, 1.73) | 0.502 | 1.30 (0.54, 3.16) | 0.560 |
| Conjunctivitis | 1.44 (0.84, 2.44) | 0.812 | 2.19 (1.24, 3.87) | 0.007 |
| Maculopathy | 0.70 (0.37, 1.70) | 0.541 | 0.97 (0.43, 2.19) | 0.934 |

4. Discussion

In this study, we collected data from 8,743 HIV-infected patients hospitalised in Guangzhou and investigated the prevalence of detected OMs determined using different ophthalmic examination modes over the 12 years of the HAART era. Our study has two significant findings. First, the implementation of routine ophthalmic examinations plays a critical role in OM detection and the management of patients with an HIV infection. Second, in HIV-infected patients, a strong correlation is observed between systemic diseases and the presence of OM.

Despite the wide accessibility of HAART in China, a high prevalence of OMs (12.8%) was still present in the routine ophthalmic examination group. Retinal disorders were seen in 8.3% of patients in the routine ophthalmic examination group (Supplementary Table 1) accounted for 64.4% of OMs, which were the primary cause of vision loss reported in previous studies [12,34]. Early diagnosis is the key to timely treatment to decrease vision loss. The implementation of routine ophthalmic examinations significantly improved the odds of OM detection by approximately 9 times, and improved the detection of three common vision-threatened OMs, keratitis, retinitis and vascular abnormalities, by 15.8–20.0 times compared to the other two groups. The increased accuracy and detection of all types of OMs in the routine ophthalmic examination group highlights the role of the ophthalmology department, ophthalmologists and examination equipment, suggesting the need for appropriate ophthalmic
examinations. Moreover, compared to the non-ophthalmologist examination group, the establishment of an ophthalmology department without routine examinations of every HIV-infected patient (as was the case for the on-demand ophthalmic examination group) did not significantly improve the detection of OMs. Therefore, both high-quality ophthalmic examinations and appropriate medical regulations are crucial for the early and accurate diagnosis of OMs in HIV-infected patients.

Notably, the changing need for hospitalisation was inversely having an influence on the prevalence of OM in our study period. The patients were admitted to the hospital with a better condition of HIV infection than before with the upgraded Guideline for AIDS management in China [32,33] emphasizing the importance of timely initiation of HAART (once the HIV infection is confirmed, the HAART should be initiated timely) and the improving capacity of the Chinese hospitals. Our study also found a decreased hospitalisation duration of hospitalised HIV-infected patients, revealing that the patients had a less severe condition than before. Moreover, the efficacy of the "Four Frees and One Care" policy for HIV-infected patients is also crucial in encouraging more patients to visit a doctor and adhere to long-term drug regimens, as early treatments lead to improved outcomes and decreased OMs [35–37]. Considering the fact that the prevalence of detected OMs ultimately increased because of the application of the routine ophthalmic examinations, we recommended that even HIV-positive individuals without a need for hospital treatment should undergo regular eye examinations because of its essential role for the early diagnosis of vision-threatening OMs.

Our results also show that patients who were older than 50 years old, males, paid with medical insurance, and that were not resident in Guangzhou, had higher odds of having OMs, which were not entirely consistent with the previous studies. Some researchers found that the increasing age was a risk factor of OMs, while sex was not associated [20]. In another study, neither ages nor sex was associated with OMs [38]. Although the floating population and medical insurance payments were not discussed in the previous studies, we noted that patients are more likely to see doctors for non-fatal complications when they have access to medical insurance [39,40]. Based on our research, future prevention and control efforts should pay attention to these populations. We will also further investigate the interaction between OMs and these demographic characteristics in the future study.

The association between systemic diseases, immunodeficiency and the presence of OM indicates that OMs represent a potential confounding factor of systemic diseases and patient immunity, adding value to the examination and diagnosis of OMs. Therefore, on the one hand, patients with documented immunodeficiency should be examined carefully for OMs. On the other hand, infectious diseases, especially the cytomegalovirus infection, are becoming a much more common cause of vision loss and blindness in eye clinic [41,42]. Missed diagnosis and misdiagnosis increased because of the growing number of HIV-infected patients [43]. One of the important reasons was that the patients came to the eye clinic without knowing their condition or deliberately concealing their history of HIV infection [44]. Therefore, to avoid missed diagnosis and misdiagnosis, patients with OMs should also focus on their systemic conditions and should undergo additional immune function tests, such as a T cell test, particularly if they are diagnosed with retinopathy or retinitis.

We constructed a model to illustrate the possible interrelationships among these factors in our study (Fig. 5). The observed prevalence of OMs is influenced by a combination of the true prevalence of OMs and their diagnosis in the real world. The OMs refer to the patients’ true eye conditions, which are influenced by treatment. The diagnosis of OMs is related to the mutual influence of external factors such as the patient’s willingness to seek ophthalmic examinations and the quality of treatment. In this study, the prevalence of OMs in the routine ophthalmic examination group reflected the true prevalence of OMs in hospitalised HIV-infected patients, whereas the prevalence was much lower in the non-routine ophthalmic examination group as a result of differences in ophthalmic examination modes, medical insurance, and other factors.

There are a few limitations in the study. First, potential factors that may affect the prevalence of detected OMs, including pregnancy [45] and drug use [46], were not characterised in our study. Second, according to the Guidelines for AIDS diagnosis and treatment in China, after 2012, the first-line HAART changed from stavudine + lamivudine + efavirenz/nevirapine to tenofovir/zidovudine + lamivudine + efavirenz/nevirapine, as stavudine was reported to cause severe adverse reactions in many cases [47]. The

![Fig. 5. The model of ocular manifestation (OM) detection and its related factors. The arrow represents having effect on the pointing object. The observed prevalence of OMs is influenced by a combination of the true prevalence of OMs and their diagnosis in the real world. The OMs refer to the patients’ true eye conditions, which are influenced by treatment. The diagnosis of OMs is related to the mutual influence of external factors such as the patient’s willingness to seek ophthalmic examinations and the quality of treatment. In this study, the prevalence of OMs in the routine ophthalmic examination group reflected the true prevalence of OMs in hospitalised HIV-infected patients, whereas the prevalence was much lower in the non-routine ophthalmic examination group as a result of differences in ophthalmic examination modes, medical insurance, and other factors.](image-url)
prevalence of detected OMs before 2012 may have been slightly influenced as well [46]. Third, although the percentage of patients with severe condition decreased, most of the hospitalised HIV-infected patients required certain inpatient treatment, indicating an overall more severe condition than the outpatients. Therefore, the results presented here may not be generalizable to the HIV-infected population overall. Fourth, this study was based on data collected from hospitalised HIV-infected patients in one of the most prosperous cities in China; therefore, the data may not wholly represent the general condition of OMs in HIV-infected patients in this country.

In conclusion, the implementation of routine ophthalmic examinations, including both high-quality ophthalmic examinations and appropriate medical regulations, is crucial for the early and accurate diagnosis of OMs in HIV-infected patients. Timely diagnosis of eye diseases may not only promote early treatment and improved prognoses but also allow patients to be alerted to additional systemic diseases. Therefore, in addition to increasing the awareness of OMs and other non-fatal complications in HIV-infected patients, we suggest ophthalmic examinations as a routine procedure to improve the early diagnosis of OMs and decrease vision loss in patients with the management of HIV infection and other chronic diseases.

Author contributions

H Lin conceived and designed the study. X Wang, W Li, D Lin, Z Liu, X Wu, J Wang, X Zhang, Y Yang, R Wang, and R Li collected and interpreted the data. W Li and L Zhao carried out the statistical analysis. W Li wrote the manuscript. H Lin, W Huang, D Lin, Y Zhu, C Chen, and X Huang reviewed and edited the manuscript. All authors have seen the final version of the manuscript and approved it for publication. The corresponding author had full access to all the data in the study and assumed final responsibility for the decision to submit the manuscript for publication.

Data sharing statement

The deidentified participant dataset are available for research purposes from the corresponding authors on reasonable request.

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Declaration of Competing Interest

The authors declare no competing financial interests.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2020.100646.

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In conclusion, the implementation of routine ophthalmic examinations, including both high-quality ophthalmic examinations and appropriate medical regulations, is crucial for the early and accurate diagnosis of OMs in HIV-infected patients. Timely diagnosis of eye diseases may not only promote early treatment and improved prognoses but also allow patients to be alerted to additional systemic diseases. Therefore, in addition to increasing the awareness of OMs and other non-fatal complications in HIV-infected patients, we suggest ophthalmic examinations as a routine procedure to improve the early diagnosis of OMs and decrease vision loss in patients with the management of HIV infection and other chronic diseases.

Author contributions

H Lin conceived and designed the study. X Wang, W Li, D Lin, Z Liu, X Wu, J Wang, X Zhang, Y Yang, R Wang, and R Li collected and interpreted the data. W Li and L Zhao carried out the statistical analysis. W Li wrote the manuscript. H Lin, W Huang, D Lin, Y Zhu, C Chen, and X Huang reviewed and edited the manuscript. All authors have seen the final version of the manuscript and approved it for publication. The corresponding author had full access to all the data in the study and assumed final responsibility for the decision to submit the manuscript for publication.

Data sharing statement

The deidentified participant dataset are available for research purposes from the corresponding authors on reasonable request.

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Declaration of Competing Interest

The authors declare no competing financial interests.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.eclinm.2020.100646.
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