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Case management strategy enhances virological response in people living with human immunodeficiency virus in a resource-limited region in Southwest China: a real-world prospective observational study

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Abstract

This study assessed the effectiveness of case management compared to that of standard care in improving treatment outcomes for first-time antiretroviral therapy (ART) patients in Liangshan Prefecture, China. First-time ART patients (total n = 828) were divided into the Standard Care Group (SCG, n = 419) and Case Management Group (CMG, n = 409). At week 48, the CMG showed higher retention rates (97.7% vs. 93.6%), better adherence, and more complete virological responses (84.2% vs. 64.0%) compared to the SCG. These findings suggest that case management improves adherence and virological suppression in resource-limited areas, though further research is needed to confirm its broader applicability.

Keywords Human immunodeficiency virus, Acquired immunodeficiency syndrome, Antiretroviral treatment, Case management, Virological response

Background

Although China has a low overall prevalence of human immunodeficiency virus (HIV), significant disparities exist. Liangshan Prefecture in Sichuan Province, marked by severe HIV endemic and low economic status, exemplifies these disparities [1, 2].

China's National Free Antiretroviral Treatment Program (NFATP), launched in 2005, enabled over 90% of people living with HIV (PLWH) in Liangshan Prefecture to receive free antiretroviral therapy (ART); however, many of these patients still struggled with virological suppression [3, 4]. In addition to drug-resistant mutations, limited access to more effective drugs and poor adherence usually resulted in virological failure or low-level viremia [5].

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Case management, usually involving professional nurses, is used in chronic disease care [6, 7] and has shown positive outcomes in developed regions [8–10]. However, its use in resource-limited areas has been less studied. Therefore, our study evaluated the effectiveness of a case management approach compared with standard care in improving patient adherence and virological response in the Liangshan Prefecture.

Methods

Study design

This prospective observational study conducted in Liangshan Prefecture allocated ART-initiating patients to the Standard Care Group (SCG) and Case Management Group (CMG). The primary endpoint was at 48 weeks, assessing retention, adherence, and virological response. A complete virological response was defined as HIV-viral load (HIV-VL) < 50 cps/mL, with an extension to 72 weeks for patients with HIV-VL ≥ 50 cps/mL at week 48. Patients with HIV-VL ≥ 1000 cps/mL underwent drug resistance testing, and regimen adjustments were made if necessary. The secondary outcome was the virological response at week 72.

Patient recruitment

Patients were recruited from 20 NFATP-designated community hospitals in Liangshan Prefecture, China. The inclusion criteria included age ≥ 15 years, ART-naïve status, total bilirubin < 95 μmol/L, alanine aminotransferase < 400 IU/L, and estimated glomerular filtration rate ≥ 30 mL/min/1.73 m^2. Patients with uncontrolled opportunistic infections or malignancies were excluded. Participants were stratified by HIV-VL (< 100,000 and ≥ 100,000 cps/mL) and balanced between SCG and CMG.

ART

Both groups received ART regimens with two nucleoside reverse transcriptase inhibitors (NRTIs) and one non-nucleoside reverse transcriptase inhibitor (NNRTI), similar to the NFATP protocol (Table 1).

Standard care

Community healthcare providers in the SCG conducted home visits or used WeChat reminders to enhance medication adherence and provide health consultations at least three times weekly.

Case management

The CMG received specialized case management from a team of two nurses, a peer educator, and a mental health counselor. Additionally, the nurses coordinated with organizations to assist with medical consultations, medications, and prenatal care. Peer educators provided monthly health education, and counselors offered psychological support as needed.

Retention evaluation

Retention was defined as the number of patients who remained on treatment and follow-up through week 48, excluding those disqualified by the study criteria. The retention rate was calculated as the proportion of patients retained at week 48, relative to the total number of initially enrolled patients, excluding disqualified cases.

Adherence evaluation

Adherence was assessed using both the Morisky Medication Adherence Scale (MMAS) and pill counting. MMAS scores range from 0 to 8, with higher scores indicating better adherence. Adherence was classified as high (MMAS score of 8 and ≥ 95% pill count), moderate (MMAS score of 6–7 and 80–94% pill count), or low (MMAS score ≤ 5 and < 80% pill count). Groups were compared based on these adherence categories.

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, N.Y., USA). Categorical variables were analyzed using a chi-square test, and continuous variables with t-test or U-test. Statistical significance was set at $P < 0.05$.

Results

Study flow and baseline characteristics of all patients enrolled in the analysis

We screened 900 patients, with 450 in each group; 31 patients were excluded from the SCG and 41 from the CMG (Fig. 1). Finally, of the 828 patients, those in the SCG (N = 419) and CMG (N = 409) were compared in terms of age, sex, education level, infection duration, transmission, body mass index, World Health Organization clinical staging, baseline HIV RNA levels, and Cluster of Differentiation 4 positive (CD4 +)T-cell counts (Table 1).

Cohort retention at week 48

The retention rate in the SCG at week 48 was 93.6% (392/419), with 27 patients lost to follow-up: 17 due to adverse drug reactions, 4 due to work migration, 2 over drug efficacy concerns, and 3 due to relocation, which prevented continued participation in follow-up, while 1 was lost for unknown reasons. In contrast, the CMG had a 97.7% retention rate (400/409), with 9 lost to follow-up: 3 due to adverse reactions, 4 due to work migration, and 2 for unknown reasons. The retention rate

Table 1 Baseline characteristics of the patients remaining in this study after 48 weeks of follow-up[‡]

	SCG (n = 392)	CMG (n = 400)	Statistic	*P*-value
Sex N (%)			$\chi^2 = 2.540$	0.111
Male	224 (57.2)	206 (51.5)		
Age (years)	35 (30–41)	36 (31–41)	Z = 1.504	0.133
Marital status N (%)			$\chi^2 = 2.466$	0.291
Single	40 (10.2)	39 (9.8)		
Married	310 (79.1)	326 (81.4)		
Divorced/widowed	42 (10.7)	35 (8.8)		
Educational level N (%)			$\chi^2 = 2.028$	0.154
Illiterate	280 (71.4)	267 (66.7)		
Body mass index (kg/m^2)	21.8 (20.2–23.1)	21.5 (19.7–23.6)	Z = – 76941	0.650
Route of infection N (%)			$\chi^2 = 1.069$	0.615
Intravenous drug use	191 (48.7)	188 (47.0)		
Heterosexual transmission	198 (50.5)	206 (51.5)		
Other	3 (0.8)	6 (1.5)		
World health organization clinical staging N (%)			$\chi^2 = 3.909$	0.142
Stage I	50 (12.7)	42 (10.5)		
Stage II	336 (85.8)	344 (86.0)		
Stage III	6 (1.5)	14 (3.5)		
Treatment regimen N (%)			$\chi^2 = 2.847$	0.416
AZT + 3TC + EFV	65 (16.6)	71 (17.8)		
AZT + 3TC + NVP	15 (3.8)	8 (2.0)		
TDF + 3TC + EFV	304 (77.6)	310 (77.5)		
TDF + 3TC + NVP	8 (2.0)	11 (2.7)		
Baseline human immunodeficiency virus RNA (Log_{10} cps/mL)			Z = 77730	0.835
Baseline CD4 + T cell count	376 (258–523)	354 (252–520)	Z = 75832	0.425

[‡] Demographic and medical characteristics in each group and the difference between the two groups

SCG Standard Care Group, *CMG* Case Management Group, χ^2 Chi-square test, *Z* Z-score, *N (%)* Number and percentage, *kg/m^2* kilograms per square meter, *AZT* Zidovudine, *3TC* Lamivudine, *EFV* Efavirenz, *NVP* Nevirapine, *TDF* Tenofovir Disoproxil Fumarate, *cps/mL* copies per milliliter, *CD4* + Cluster of Differentiation 4 positive

was significantly higher in the CMG than in the SCG ($\chi^2 = 8.961$, $P = 0.003$).

Adherence and therapeutic response at week 48

Adherence and HIV-VL were assessed in the remaining patients at 48 weeks. First, we analyzed the baseline characteristics of the patients retained at follow-up. No significant differences were found in demographic and medical characteristics between the two groups (Table 1).

In the SCG (N = 392), 239 patients (61.0%) had high adherence, 16 (4.1%) had moderate adherence, and 137 (34.9%) had low adherence. In the CMG (N = 400), 317 patients (79.3%) achieved high adherence, 20 (5.0%) had moderate adherence, and 63 (15.7%) had low adherence. The CMG had significantly more patients with high adherence ($\chi^2 = 31.628$, $P < 0.01$) and significantly higher overall adherence compared with the SCG ($\chi^2 = 41.288$, $P < 0.01$).

The virological response was higher in the CMG (84.2%, 337/400) than in the SCG (64.0%, 251/392). Additionally, the median CD4 + T-cell count in the SCG increased from 376 (258–523) at baseline to 381 (247–519) at week 48. However, it increased from 354 (252–520) at baseline to 423 (289–584) at week 48 in the CMG. The CD4 + T-cell count was significantly higher in the CMG than in the SCG (Z = – 3.114, $P = 0.02$).

Drug resistance test and regimen adjustment at week 48

At week 48, of the 204 patients without complete virological response, 75 underwent resistance testing. In 20.0% (15/75) of patients, resistance-related mutations were observed in both NRTI and NNRTI regions and 52.5% (39/75) in the NNRTI region alone. Patients with known resistance mutations switched to the second-line regimen (Tenofovir Disoproxil Fumarate + Lamivudine + Lopinavir/Ritonavir), while others continued their initial regimen. All 204 patients were managed for 72 weeks according to their original group assignments.

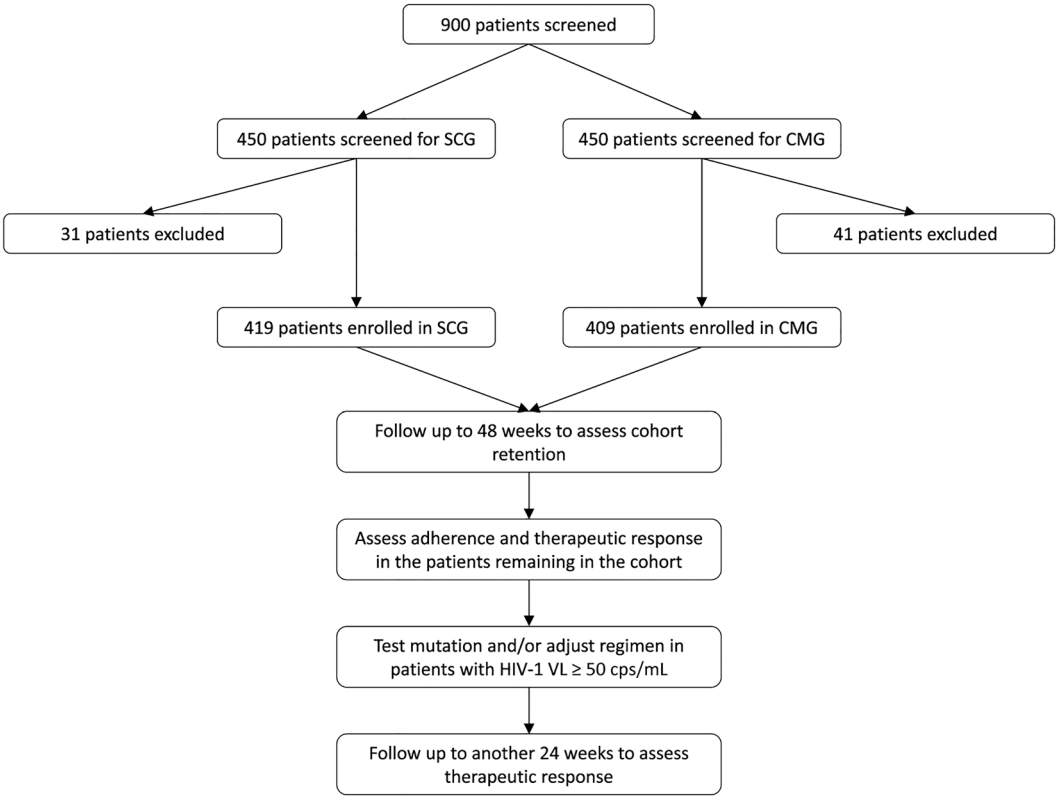

Fig. 1 Flowchart of patient enrollment and follow-up. A total of 900 patients were screened, and 828 were enrolled for a 48-week follow-up and assessment. Furthermore, 24-week follow-ups were scheduled for patients with suboptimal virological responses. *SCG* Standard Care Group, *CMG*: Case Management Group, *HIV-1* human immunodeficiency virus type 1, *VL* viral load.

Virological response at week 72 in patients with suboptimal response at week 48

Over the 24-week follow-up period, no patient was lost to follow-up. HIV-VL testing was repeated at 72 weeks. In the CMG, 63.5% (40/63) of patients achieved a complete virological response, compared to 38.3% (54/141) in the SCG. The CMG exhibited significantly better virological outcomes than the SCG after regimen adjustment ($\chi^2 = 11.124$, $P = 0.001$).

Discussion

Liangshan Prefecture, one of China's least developed areas, faces ongoing issues of scarce resources and high HIV prevalence [11, 12]. Despite NFATP, which enabled over 90% of PLWH to receive antiretroviral treatment [13], many of them do not achieve satisfactory virological responses [14, 15]. The current management model in Liangshan Prefecture includes centralized medication distribution and periodic testing. However, daily patient management is left mainly to unskilled community health care providers and limits comprehensive care.

Case management is a recognized effective model for chronic disease management [16]. Our study showed that it improves treatment retention, adherence, and response among ART-initiating patients in resource-scarce regions, particularly those failing their initial regimen. Therapeutic outcomes were more favorable in the CMG than in the SCG after regimen adjustments, regardless of the mutation status.

This is the first study to evaluate case management in a resource-limited area of China. We formed a skilled team to advocate for patients; assist with medication access; manage adverse reactions; provide testing, consultations, and psychological support; and facilitate family and social support. This multifaceted approach enhanced adherence to treatment. Therefore, our findings will improve HIV management strategies in this region and serve as a reference for similar areas.

This study has limitations. First, better treatment adherence among participants may introduce selection bias, limiting the generalizability of the findings. Additionally, reliance on self-reported data and varying experience of community healthcare providers may affect data accuracy. Since this study was conducted in one region, its applicability to other areas with different healthcare infrastructures and cultural

contexts remains uncertain. Therefore, further longitudinal research in diverse resource-limited settings is needed to validate the broader effectiveness of case management.

In conclusion, our study suggests that case management may enhance treatment adherence and virological suppression in resource-limited areas like Liangshan Prefecture. Nonetheless, additional studies are required to explore its long-term benefits and potential adaptability across different contexts.

Abbreviations

3TC	Lamivudine
ART	Antiretroviral therapy
AZT	Zidovudine
CMG	Case management group
HIV	Human immunodeficiency virus
HIV-VL	HIV viral load
LPV/r	Lopinavir/Ritonavir
NFATP	National free antiretroviral treatment program
NNRTI	Non-nucleoside reverse transcriptase inhibitor
NRTI	Nucleoside reverse transcriptase inhibitor
PLWH	People living with HIV
SCG	Standard care group
TDF	Tenofovir disoproxil fumarate

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Author contributions
Conceptualization, LC and HT; Methodology, XS and JZ; Software, JW and LD; Investigation, FM and CL; Resources, HT; Data Curation, XS; Writing—Original Draft Preparation, XS and JZ; Writing—Review and Editing, LC; Visualization, LC; Project Administration, HT; Funding Acquisition, HT.

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Availability of data and materials
The data supporting the conclusions of this study are presented in the main manuscript. Any additional data can be obtained by contacting the corresponding author.

Declarations

Ethics approval and consent to participate
The study received approval from the Medical Ethics Committee of West China Hospital, Sichuan University (Annual Review No. 450, version 2019.5). Informed consent was obtained from all participants. The study was retrospectively registered on 2023–09-28 (ChiCTR2300076265).

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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