# The Effects of Health Education on Acute Intermittent Porphyria Attacks : A Retrospective Cohort Study

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**Research Article**

**Additional Declarations:** No competing interests reported.

# Abstract

**Background:** Acute Intermittent Porphyria (AIP) is characterized by acute attacks of neurovisceral symptoms. Infection and negative emotions are factors that can trigger acute AIP attacks, thus avoiding these potential triggers can effectively reduce the risk of acute attacks. During the COVID-19 pandemic, online health education provides patients with a convenient and safe way to receive health education, thus effectively improving their quality of life QoL . We explored the effect of online health education on acute AIP attacks during the COVID-19 pandemic.

**Methods** This study retrospectively included 47 patients with AIP who were infected with COVID-19 and completed a questionnaire from November 2022 to March 2023. These participants were divided into two groups based on whether they had received centralized health education during COVID-19. The primary outcomes were acute AIP attacks, AIP attack severity, and QoL. Secondary outcomes were negative emotions and positive coping styles.

**Results:** In comparison to the non-health education group, the health education group showed a significant decrease in the incidence of acute AIP attacks ($P < .05$), a reduction in the severity of AIP attacks ($P < .05$), and an improvement in QoL ($P < .05$). Additionally, the health education group had a significant decrease in negative emotions ($P < 0.05$) and a substantial increase in positive coping styles ($P < 0.05$).

**Conclusions:** Health education may enhance patients' cognition and coping skills, and reduce negative emotions, thereby reducing the occurrence and severity of acute AIP attacks, and improving the patients' QoL.

# Introduction

Acute intermittent porphyria (AIP) is a rare, autosomal dominant, inherited metabolic disease [1]. The acute attacks of AIP are usually induced by infection, drugs, progesterone fluctuations, and negative emotions, and are often clinically manifested as serious neurovisceral symptoms, and can even be life-threatening in severe cases. Therefore, taking active measures to avoid these potential triggers can effectively prevent the acute attack of AIP and reduce its severity. Health education is an effective tool for improving patients' understanding and self-management skills, helping them to actively avoid risk factors and improve their prognosis and quality of life (QoL). In recent years, it has been widely used in the prevention and treatment of chronic illnesses such as diabetes and hypertension [2,3]. In light of the COVID-19 pandemic, online health education offers convenience, a wealth of resources, interactivity, and wide dissemination, thus improving the quality and efficiency of education and promoting public health [4,5]. As a particularly vulnerable group, patients with rare diseases are often more susceptible to the impact of viruses than the general population. During the COVID-19 pandemic, they have faced even greater challenges [6]. It has been reported in the literature that COVID-19 can trigger severe acute attacks of AIP, therefore, close monitoring of AIP patients is recommended during the epidemic period [7].

However, this study did not propose specific solutions for managing AIP patients during the COVID-19 outbreak. Therefore, this study aims to explore the effect of online health education on the acute attack of AIP in AIP patients with COVID-19 infection through a retrospective cohort study, providing a reference for optimizing clinical strategies for preventing the acute onset of AIP.

# Materials and Methods

Study Participants

This study was conducted utilizing the Porphyria Multidisciplinary Teamwork (MDT) Database of the Second Hospital of Hebei Medical University. This study included patients with AIP who had contracted COVID-19, completed the questionnaire, and met the inclusion and exclusion criteria between November 2022 to March 2023. Patients were classified into two groups: the health education group and the non-health education group, based on whether they had received intensive health education during the COVID-19 period.

The inclusion criteria were as follows: (1) Diagnosis of AIP through genetic analysis; (2) Clear consciousness, normal cognition, and no communication barriers; (3) Complete information; (4) Ability to use smartphones, WeChat, and other social media platforms by either the patient or their family members.

The exclusion criteria were as follows: (1) History of psychiatric disorders, alcohol, or drug addiction; (2) Coexisting severe medical conditions, such as cancer, liver, or kidney failure; (3) Lack of essential information; (4) Participation in other clinical research studies.

Ultimately, this research included 47 AIP patients, of whom 35 were in the health education group and 12 were in the non-health education group. The attrition rate was 7.8%, and the flow of the study is depicted in Figure 1. It was approved by the Ethics Review Committee of the Second Hospital of Hebei Medical University (2023-R597) and followed the Helsinki Declaration. As it was a retrospective study, informed consent was not required.

Health Education

The Porphyria MDT Health Education Team of the Second Hospital of Hebei Medical University organized and carried out a two-month health education program that included disease knowledge propaganda and education, psychological health guidance, and medical-patient interaction via WeChat. All patients received notifications at the beginning of the program; however, some were unable to take part due to various reasons and were consequently included in the non-health education group.

(1) Health education team

The health education team is comprised of a chief physician, an associate chief physician, three attending physicians, three resident physicians, and a psychological counselor, all of whom have

considerable experience in AIP patient management and have received specialized training.

(2) Health education content

### Disease knowledge propaganda and education

Every other week, an online lecture is held to educate patients on the basic knowledge of AIP, including its etiology, pathogenesis, clinical manifestations, treatments, and prevention. Patients are helped to understand the common triggers for acute attacks (such as medications, infections, and emotions) and learn methods to avoid triggers, recognize precursors and early symptoms of AIP, and handle them effectively. In addition, patients are instructed on how to prevent COVID-19 and provided with guidance on safe medication after infection.

### Psychological health guidance

Every other week, psychological counseling is provided to patients. Firstly, patients are assisted in understanding the root cause of their negative emotions and guided to express their emotions and respond to the disease with a positive and calm attitude. Secondly, patients are encouraged to actively regulate their own emotions and taught relaxation techniques such as attention diversion and emotional regulation methods to help them self-adjust. Finally, the mental health status of AIP patients is evaluated, and individualized guidance and treatment is provided for those with mental health issues.

### Medical-patient WeChat interaction platform

A medical-patient WeChat interaction platform has been established to ensure that patients can stay in touch with the medical team at all times. AIP and COVID-19 related knowledge is regularly sent to patients through the WeChat platform, and online interactions are conducted with them to promptly answer their questions and provide guidance.

Data collection and evaluation

Retrospective collection of patient information from the database, including demographic data (gender, age, education level, marital status, and employment status), participation in health education, acute attacks of AIP, and severity of attack during the follow-up period. Additionally, data on negative emotions, positive coping styles, and QoL of patients at baseline and the end of the follow-up period were collected.

(1) Assessment of acute AIP attacks and severity

Acute attacks of AIP are defined as a combination of episodic symptoms of pain, autonomic nervous system disturbance, peripheral neuropathy, and central nervous system dysfunction, requiring hospitalization or emergency treatment, intravenous heme infusion, or high-dose glucose therapy [8,9]. The severe acute attack of AIP is characterized by one or more of the following features: severe hyponatremia (serum sodium <125 mmol/L), peripheral neuropathy (limb paresis), central nervous

system involvement (seizures, respiratory distress, and altered consciousness), and cardiac arrhythmias [10].

(2) Assessment of the quality of life

The Short Form 36-item Health Survey (SF-36) was employed to evaluate the QoL of AIP patients. This questionnaire consists of eight dimensions: physical functioning (PF), role physical (RP), body pain (BP), general health (GH), vitality (VT), social functioning (SF), role emotional (RE), and mental health (MH) [11]. All dimensions can be aggregated into two component summary scales: the physical component summary (PCS) score for assessing physical health and the mental component summary (MCS) score for assessing mental health. A higher score corresponds to a QoL.

3 Assessment of negative emotions

The Positive and Negative Affect Scale (PANAS) and the Depression Anxiety Stress Scale-21 (DASS-21) were utilized to assess the emotional states of individuals with AIP. The PANAS consists of 20 questions, divided into two emotional categories: a positive sentiment and a negative sentiment, rated using a five-point Likert scale [12]. The DASS-21 is a tool with three sub-scales that assesses depression, anxiety, and stress [13]. It consists of 21 items, each of which is rated from 0 (not applicable) to 3 (highly applicable).

(4) Assessment of positive coping styles

To assess the reactions and attitudes of patients when faced with difficulties or challenges, the Simplified Coping Style Questionnaire (SCSQ) [14] was utilized. This questionnaire has two dimensions: positive coping and negative coping, comprising a total of 20 items. Each item is scored from 0 (seldom adopted) to 3 (frequently adopted).

## Statistical analysis

Data analysis was performed using SPSS 26.0 statistical software. Quantitative data were expressed as means and standard deviations ($\bar{x} \pm s$), and intergroup comparisons were conducted using independent sample t-tests. Categorical data were expressed as frequencies and percentages (n (%)), and intergroup comparisons were conducted using Chi-square tests or Fisher's exact tests. Internal consistency of the scale was assessed through Cronbach's α analysis, and $p < 0.05$ was considered a statistically significant difference.

# Results

## Baseline characteristics of participants

This study included 47 AIP patients, with 35 receiving health education and 12 not receiving it. The baseline of the two groups was relatively equal in terms of gender, age, education level, marital status,

and employment status, and no statistically significant differences were observed between them ($p >$ 0.05), as Table 1 demonstrates.

Table 1  Baseline characteristics of Health Education *vs.* Non-Health Education groups

|  | Health Education n=35 | Non-Health Education n=12 | p |
|---|---|---|---|
| Sex |  |  | 1.00 |
| Male | 0  0% | 0  0% |  |
| Female | 35  100% | 7  100% |  |
| Age year | 31.83±6.43 | 28.08±8.49 | 0.116 |
| Educational level |  | 2.400 | 0.470 |
| High school and below | 10  28.6% | 2  16.7% |  |
| Junior college | 17  48.6% | 5  41.7% |  |
| Bachelor and above | 8  22.9% | 5  41.7% |  |
| Marital status |  |  | 0.569 |
| Single | 11  31.4% | 5  41.7% |  |
| Married | 22  62.9% | 6  50% |  |
| Divorced | 2  5.7% | 1  8.3% |  |
| Working status |  |  | 0.253 |
| Employed | 14  40% | 5  41.7% |  |
| Unemployed | 16  45.7% | 3  25.0% |  |
| Attend school | 5  14.3% | 4  33.3% |  |

Effect of health education on acute AIP attacks and severity

The health education group with AIP showed a significantly reduced incidence of acute attacks compared to the non-health education group (48.6% *vs.* 83.3%, OR=0.189, 95% CI: 0.036—0.990, $p$ = 0.036). Furthermore, the health education group exhibited significantly lower incidences of severe symptoms, including limb paralysis (5.7% *vs.* 50%, OR = 0.061, 95% CI: 0.010—0.375, $p$ = 0.002), seizures (2.9% *vs.* 25%, OR = 0.088, 95% CI: 0.008—0.953, $p$ = 0.046), dyspnea (5.7% *vs.* 41.7%, OR = 0.085, 95% CI: 0.014—0.530, $p$ = 0.008), and disturbance of consciousness (2.9% *vs.* 33.3%, OR = 0.059, 95% CI: 0.006—0.600, $p$ = 0.013), as shown in Table 2.

Table 2  Acute attacks and severity of AIP in Health Education *vs.* Non-Health Education groups

|  | Health Education n=35 | Non-Health Education n=12 | OR (95% CI) | p |
|---|---|---|---|---|
| Acute attack | 17/35 48.6% | 10/12 83.3% | 0.189 0.036–0.990 | 0.036* |
| Main manifestation | | | | |
| Abdominal pain | 19/35 54.3% | 9/12 75% | 0.396 0.091–1.715 | 0.310 |
| Nausea /Vomiting | 17/35 48.6% | 9/12 75% | 0.315 0.073–1.363 | 0.112 |
| Constipation | 12/35 34.3% | 8/12 66.7% | 0.462 0.110–1.936 | 0.286 |
| Ileus | 13/35 37.1% | 8/12 66.7% | 0.542 0.129–2.272 | 0.399 |
| Arrhythmology | 6/35 17.1% | 4/12 33.3% | 0.414 0.093–1.832 | 0.251 |
| Hypertension | 6/35 17.1% | 4/12 33.3% | 0.414 0.093–1.832 | 0.251 |
| Hyponatremia | 6/35 17.1% | 5/12 41.7% | 0.290 0.068–1.229 | 0.118 |
| Quadriplegia | 2/35 5.7% | 6/12 50% | 0.061 0.010–0.375 | 0.002* |
| Epilepsy | 1/35 2.9% | 3/12 25% | 0.088 0.008–0.953 | 0.046* |
| Dyspnea | 2/35 5.7% | 5/12 41.7% | 0.085 0.014–0.530 | 0.008** |
| Disorder of consciousness | 1/35 2.9% | 4/12 33.3% | 0.059 0.006–0.600 | 0.012* |

## Effect of health education on QoL

The SF-36 questionnaire displayed no statistically significant deviation in the baseline scores between the two groups ($p > 0.05$). The Cronbach's α for the SF-36 questionnaire was 0.873, which suggests an excellent internal consistency. At the end of the follow-up period, compared to the non-health education group, the health education group exhibited a significant increase in both PCS (61.29 ± 19.36 *vs.* 48.23 ± 17.34, $p = 0.045$) and MCS scores (65.47 ± 15.01 *vs.* 52.94 ± 14.04, $p = 0.015$). Results from the detailed data showed that the health education group had significantly greater improvements in PF (77.14 ± 22.40 *vs.* 58.33 ± 24.34, $p = 0.018$), BP (63.14 ± 20.11 *vs.* 42.50 ± 22.41, $p = 0.005$), VT (52.57 ± 11.84 *vs.* 38.22

± 8.07, $p$ = 0.000), and MH scores (56.46 ± 11.26 $vs$. 43.67 ± 10.44, $p$ = 0.001) when compared to the non-health education group, as shown in Table 3.

Table 3 Scores of SF-36 in Health Education $vs$. Non-Health Education groups

| | Baseline Score | | | Follow-up Score | | |
|---|---|---|---|---|---|---|
| | Health Education n=35 | Non-Health Education n=12 | $p$ | Health Education n=35 | Non-Health Education n=12 | $p$ |
| PCS | 63.03±16.04 | 65.52±10.26 | 0.541 | 61.29±19.36 | 48.23±17.34 | 0.045* |
| PF | 84.00±16.88 | 89.17±8.48 | 0.317 | 77.14±22.40 | 58.33±24.34 | 0.018* |
| RP | 51.57±41.10 | 50.83±20.65 | 0.936 | 51.43±45.75 | 38.33±27.41 | 0.245 |
| BP | 63.14±20.26 | 71.67±13.37 | 0.182 | 63.14±20.11 | 42.50±22.41 | 0.005** |
| GH | 53.43±20.10 | 50.42±12.70 | 0.630 | 53.43±15.28 | 53.75±13.84 | 0.949 |
| MCS | 72.13±16.35 | 76.50±0.90 | 0.125 | 65.47±15.01 | 52.94±14.04 | 0.015* |
| VT | 58.00±12.90 | 60.83±12.22 | 0.509 | 52.57±11.84 | 38.22±8.07 | 0.000*** |
| SF | 81.76±34.32 | 79.79±12.81 | 0.720 | 82.14±21.07 | 81.67±10.46 | 0.919 |
| RE | 77.31±34.83 | 84.42±28.60 | 0.528 | 70.71±40.92 | 48.08±41.28 | 0.106 |
| MH | 71.43±12.50 | 79.33±14.95 | 0.079 | 56.46±11.26 | 43.67±10.44 | 0.001** |

**Effect of health education on emotions and coping styles**

Results showed no statistically significant differences in the baseline scores of the PANAS and DASS-21 questionnaires between the two groups ($p$ > 0.05). The Cronbach's α for the PANAS questionnaire was 0.822, while for the DASS-21 questionnaire, it was 0.937, suggesting a good internal consistency for both scales. After the follow-up period, the health education group exhibited a considerable decrease in the scores of the negative emotions (25.00 ± 4.81 $vs$. 29.17 ± 2.55, $p$ = 0.001), anxiety (5.49 ± 1.34 $vs$. 6.83 ± 1.40, $p$ = 0.009), and depression (4.97 ± 1.38 $vs$. 6.42 ± 1.24, $p$ = 0.003) subscales, when compared to the non-health education group. The scores of the remaining subscales did not show any statistically significant differences between the two groups ($p$ > 0.05), as shown in Table 4.

Table 4  Scores of PANAS and DASS-21 in Health Education $vs$. Non-Health Education groups

| | | Baseline Score | | | Follow-up Score | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| | | Health Education n=35 | Non-Health Education n=12 | $p$ | Health Education n=35 | Non-Health Education n=12 | $p$ |
| PANAS | | | | | | | |
| | Positive | 27.71±6.71 | 30.08±8.16 | 0.323 | 25.69±7.05 | 22.83±5.97 | 0.216 |
| | Negative | 22.80±6.28 | 21.67±6.33 | 0.593 | 25.00±4.81 | 29.17±2.55 | 0.001** |
| DASS-21 | Anxiety | 4.31±3.88 | 4.08±3.65 | 0.858 | 5.49±1.34 | 6.83±1.40 | 0.009** |
| | Depressed | 2.89±3.00 | 3.83±3.81 | 0.383 | 4.97±1.38 | 6.42±1.24 | 0.003** |
| | Stress | 3.89±3.34 | 3.86±2.52 | 0.961 | 4.03±2.66 | 3.92±3.50 | 0.908 |

The baseline scores of the SCSQ questionnaire did not demonstrate a statistically significant difference between the two groups, with $p > 0.05$. Furthermore, the SCSQ questionnaire had a satisfactory internal consistency, as indicated by its Cronbach's α of 0.814. After the follow-up period, the health education group presented a considerable increase in scores for the positive coping subscale (1.81 ± 0.49 *vs*. 1.18 ± 0.26, $p$ = 0.000) compared to the non-health education group. On the other hand, the health education group also showed a substantial decrease in scores for the negative coping subscale (1.18 ± 0.33 *vs*. 1.88 ± 0.49, $p$ = 0.000), as demonstrated in Table 5.

Table 5  Scores of SCSQ in Health Education *vs*. Non-Health Education groups

| | | Baseline Score | | | Follow-up Score | | |
| --- | --- | --- | --- | --- | --- | --- | --- |
| | | Health Education n=35 | Non-Health Education n=12 | $p$ | Health Education n=35 | Non-Health Education n=12 | $p$ |
| SCSQ | Positive coping | 1.43±0.63 | 1.28±0.39 | 0.464 | 1.81±0.49 | 1.18±0.26 | 0.000*** |
| | Negative coping | 1.30±0.31 | 1.20±0.44 | 0.380 | 1.18±0.33 | 1.88±0.49 | 0.000*** |

# Discussion

The clinical manifestation of AIP is diverse, with severe acute attacks often threatening life. Infection and negative emotions are necessary conditions for the acute attack of AIP [15], thus avoiding potential triggers can be an effective way to reduce and alleviate acute attacks of AIP. As a special group, AIP patients are more susceptible to the impact of the sudden public health event of COVID-19. Firstly, in terms of COVID-19 infection, this study found that about 61.9% (26/42) of AIP patients experienced acute attacks after COVID-19 infection, which is consistent with the research results of Bardak et al. [7]. Secondly, in terms of negative emotions, during the COVID-19 epidemic, fear, anxiety, worry, and other emotions have significantly increased in different populations [16], which may further increase the risk of acute attacks in AIP patients. Given that health education has played an important role in the prevention and treatment of chronic diseases, resulting in significant improvements in recent years, we speculate that it may be an effective measure to improve cognitive and self-management abilities in AIP patients, reduce the risk of acute attacks, and improve their QoL. This retrospective study conducted a preliminary exploration to test this speculation.

The primary outcome of this study indicates that, during the COVID-19 pandemic, health education significantly reduced acute attacks in AIP patients, reduced the severity of such attacks, and improved their QoL. Moreover, health education was effective in aiding AIP patients in adopting more positive coping styles and alleviating negative emotions. Research has demonstrated that sociodemographic factors are influential in the context of health-related behaviors [17,18], and may also have an impact on the efficacy of health education interventions. This study enhanced the reliability of the results by balancing differences in baseline characteristics such as gender composition, age, educational level, marital status, and employment status between the two groups.

The health education content of this study was rationally and scientifically designed, producing the remarkable outcomes mentioned. Specifically, disease knowledge education increases patients' understanding of AIP diseases by improving their cognitive level [19], thus allowing them to actively engage in self-management and take effective risk avoidance measures. Mental health guidance can bolster a patient's sense of self-efficacy, augment their capacity to cope with difficult situations, and assist in regulating emotions, thereby improving their emotional well-being and psychological stability[20]. The application of the medical-patient WeChat interactive platform ensures patients to stay connected with the medical team at any time, thereby providing timely guidance and management for patients to avoid acute attacks of AIP.

Our research is significant in the following aspects. Firstly, during the COVID-19 pandemic, AIP patients often struggle to receive timely and adequate medical care due to measures such as resource constraints and social isolation. At the same time, they are at risk of infection and enduring significant psychological stress, which can all contribute to an increased risk of fatal acute attacks in AIP patients. Therefore, providing health education to AIP patients is extremely urgent. This is the first time we have observed its effectiveness, providing a reference for responding to public health emergencies. Secondly, this study

explored the effect of health education on AIP patients and found that it has multiple benefits, including reducing acute attacks, alleviating the severity of attacks, and improving quality of life. These findings provide effective methods for preventing acute attacks and practical guidance for clinicians and patients. Finally, this study employed an online health education approach that fully accounted for the dispersed nature of rare disease patients, enabling efficient and widespread information dissemination while also providing greater convenience. This strategy effectively improved the utilization of disease-related knowledge and presented new strategies and methods for patient health education and follow-up, making it clinically valuable for promotion.

There are certain limitations in this study. Firstly, the health education in this study still needs further optimization. Future optimization measures can include increasing the diversity of health education content, flexible scheduling of the health education time and frequency, strengthening the co-creation process with patients, and long-term tracking and evaluation of the effectiveness of the health education to develop health education plans that are more in line with the patients' needs. Secondly, the scales used in this study were self-administered questionnaires, and the results may be subject to some subjective bias. In the future, a comprehensive evaluation using other assessment methods can be conducted to obtain more comprehensive information. Finally, this study was a single-center retrospective study with a limited number of cases, and therefore still requires multi-center prospective studies for validation.

## Conclusion

Health education may enhance patients' cognition and coping skills, and reduce negative emotions, thereby reducing the occurrence and severity of acute AIP attacks, and improving patients' QoL. Health education can serve as a preventive measure against acute AIP attacks, with significant online effectiveness, making it worthy of clinical promotion.

## Abbreviations

| | | | |
|---|---|---|---|
| AIP: | Acute intermittent porphyria ; | QoL: | Quality of life; |
| MDT: | Multidisciplinary Teamwork ; | SF-36: | Short Form 36-item Health Survey; |
| PF: | Physical functioning | RP: | Role physical ; |
| BP: | Body pain ; | GH: | General health; |
| VT: | Vitality ; | SF | Social functioning ; |
| RE: | Role emotional; | MH: | Mental health; |
| PCS: | Physical component summary; | MCS: | Mental component summary; |
| PANAS: | Positive and Negative Affect Scale; | DASS-21: | Depression Anxiety Stress Scale-21; |
| SCSQ: | Simplified Coping Style Questionnaire | | |

# Declarations

## Supplementary Material

The online version contains supplementary material available.

## Author contributions

Lanlan Zhao: manuscript writing and data management. Jie Li, Pei Li, Xin Zhao, Ningzhen Ma:collect information and data from patients. All authors reviewed the manuscript.

## Availability of data and materials

Data that supports the findings of this study are within the article. Further data is available from the corresponding author upon reasonable request.

## Ethics approval and consent to participate

We declare the study did not violate any human or animal rights. The study was approved by the Ethics Review Committee of the Second Hospital of Hebei Medical University (2023-R597).

## Consent for publication

Not applicable.

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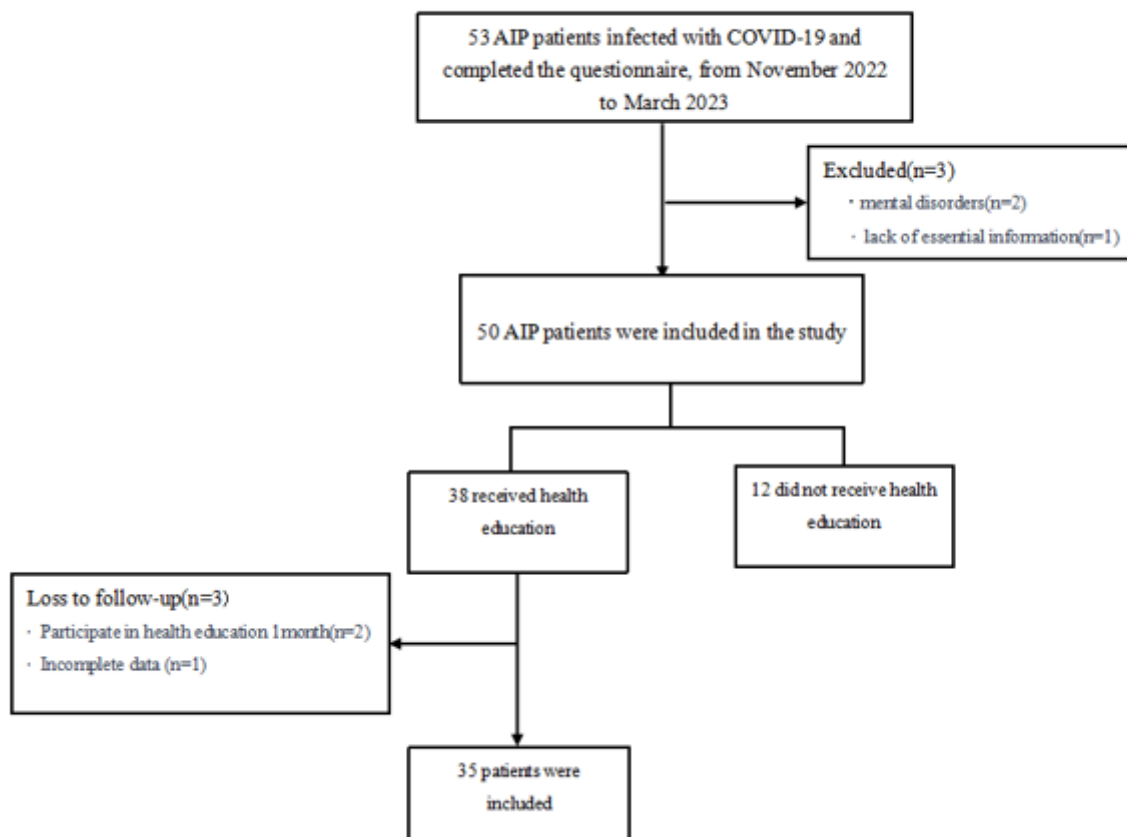
# Figures



**Figure 1**

Flow chart of this study

# Supplementary Files

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