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### *Observational Study*

**Validity of the Patient Health Questionnaires (PHQ-2 and PHQ-9) for Screening Depression among HIV patients in Lahore, Pakistan**

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### **Abstract**

#### **BACKGROUND**

Many HIV-infected patients suffer from depression, but a little focus is given to detecting and treating depression in primary health care. Detection of depression can be improved by introducing short, reliable, and valid screening instruments.

#### **AIM**

The current study assessed the psychometric properties of the PHQ-2 and PHQ-9 for depression screening and diagnosis and estimated the sensitivity and specificity of the PHQ-2 for depression screening in HIV-infected patients.

#### **METHODS**

A cross-sectional study was conducted on 158 HIV-infected patients aged 18 years and above in Lahore, Pakistan. PHQ-2 was implemented to screen depression. PHQ-9 was implemented to diagnose major depressive disorder (MDD) as a reference standard. Reliability, Validity tests and receiver operating characteristic (ROC) curve were computed.

#### **RESULTS**

The Cronbach's alpha of PHQ-2 and PHQ-9 were 0.732 and 0.759, respectively. The study results showed that the score of 2 on PHQ-2 indicates the highest Youden's index of 0.924, with both sensitivity and specificity of 0.96, and the area under the curve for PHQ-2 was 0.98 (95%CI: 0.953-0.998).

## **CONCLUSION**

The PHQ-2 and PHQ-9 demonstrated good psychometric properties, suggesting their potential benefit as tools for depression screening and diagnosis in the HIV-infected population.

## **INTRODUCTION**

People living with HIV infection (PLWHA) seem to be more vulnerable to psychiatric morbidity than the overall population [1,2], with major depressive disorder seems to be the most prevalent psychiatric diagnosis. Suicidal thinking, anxiety, post-traumatic stress disorder (PTSD), and drug/alcohol use disorders are also frequently documented psychiatric morbidities in HIV patients [3,4]. Depression is a widespread illness globally, affecting approximately 3.8 percent of the population, including 5.0 percent of adults and 5.7 percent of persons over 60. Depression affects around 280 million people worldwide [5]. The global HIV/AIDS 2020 research estimated that 37.7 million people were infected with HIV infection. Sub-Saharan Africa was linked to about two-thirds of the world's HIV-positive individuals [6]. In Pakistan, an estimated 183,705 people infected with HIV by 2020 [7]. Even though the expected prevalence of HIV infection in Pakistan's general population is less than 0.1 percent in 2019, it remains a major public health issue [8].

Depression is a mental health condition defined by a depressed mood, low mood, difficulty concentrating, self-blame or poor self-worth, sleeping or eating difficulties, and impaired focus [9, 10,11]. Depression is associated with several clinical and socio-demographic factors in HIV patients. Some clinical factors, such as AIDS-related stigma,

compromised immune status (low CD4 counts), and opportunistic infections <sup>[12,13]</sup> could be distinctive to HIV patients; however, socio-demographic factors such as gender, low levels of education, and unemployment were linked to depression including both HIV positive and negative populations <sup>[14]</sup>. Untreated depression causes rapid HIV infection advancement and increases deaths <sup>[15]</sup>. Inflammatory pathway indicators, such as monocytes and pro-inflammatory cytokines, are recognized as contributing to the higher prevalence of depression in HIV-positive individuals <sup>[16]</sup>. HIV infection <sup>7</sup> increases the production of pro-inflammatory cytokines such as Interleukin-6 (IL-6) and Tumor Necrosis Factor (TNF), which promote viral replication and CD4 cell depletion <sup>[17]</sup>.

Antidepressants were the most frequently recommended drugs, followed by anxiolytics, antipsychotics and psycho-stimulants <sup>[18]</sup>. Non-invasive brain stimulation (NIBS) techniques <sup>9</sup> such as repeated trans-cranial magnetic stimulation (rTMS) and trans-cranial direct current stimulation (tDCS) are increasingly being used to improve cognitive function and reduce depressive symptoms in a variety of settings <sup>[19]</sup>. Given that severe depression is typically associated with cognitive impairments, the NIBS method may be beneficial in enhancing cognition in depressed people <sup>[20]</sup>. More than half of the patients with a serious depressive illness did not use antidepressants. Effective depression treatment may be crucial for increasing HIV medication adherence and clinical outcomes, possibly in combination with adherence supports <sup>[21]</sup>.

Despite successful pharmacological and psychological treatments, a high proportion of individuals suffering from depression in HIV-infected patients is frequently undiagnosed clinically and is frequently untreated in primary health care settings <sup>[22, 23]</sup>. Several screening questionnaires have been developed as instruments to assist in the timely identification of depression and clinical judgment <sup>[24-28]</sup>. To generate accurate clinical results, the validity and reliability of the depression screening tools should be good. Screening tools should be easy and quick for successful practical application <sup>[29, 30, 31]</sup>. The Patient Health Questionnaire (PHQ-2 and PHQ-9) were designed especially as

depression screening and diagnostic tools for primary care settings to promote the delivery of evidence-based psychiatric care intervention strategies in regions where specially trained mental health providers are scant [32-34].

A cross-culturally applicable form of PHQ-9 and PHQ-2 is available, but its psychometric properties are still to be validated formally. In many studies, the accuracy of PHQ-9 has been tested by applying it to many chronic disease populations [35-40]. However, the PHQ-9 and PHQ-2 have not yet been validated in HIV patients in Pakistan. Therefore, the present study aimed to measure the (1) psychometric properties of the PHQ-9 and PHQ-2 for the diagnosis of depression and (2) to estimate PHQ-2 screening accuracy by using PHQ-9 as the reference standard in patients of HIV infection in Lahore, Pakistan.

## **MATERIALS AND METHODS**

### **Study setting**

The study was carried out in the HIV clinic of Jinnah hospital Lahore, Pakistan, from January 2019 to March 2019. HIV clinic in Jinnah hospital Lahore works from Monday to Saturday and serves around 20 to 30 patients per day. The population of Lahore is 11,126,285, and it is one of the most populated cities in Punjab Province [41]. The current study comprises finding active cases of depression by the use of PHQ-2 for screening, followed by the use of PHQ-9 to detect depression. Patients with a PHQ-9 score of nine or higher were referred to a psychiatrist to confirm the diagnosis of depression.

### **Study design**

An analytical cross-sectional study design was executed to assess the validity and reliability of the Patient Health Questionnaire (PHQ-9) among HIV patients.

### **Participants**

One hundred and fifty-eight study participants were recruited from the HIV clinic of Jinnah hospital, Lahore, through a non-probability convenience sampling technique. All participants were agreed to participate in the study. Eligibility criteria for study subjects

included age more than 18 years, capability to correspond, understand Urdu language, patients must have a diagnosis of HIV based on positive test on an ELISA for HIV antibodies, were attending the HIV clinic for medical care, and were available for a 20 min interview. Participants who had other medical disorders unrelated to HIV, such as renal failure, chronic hepatitis, and malignancy determined on history and clinical examination, were excluded.

## Measures

### PHQ-9

It is a nine-component criterion-based diagnostic instrument for the evaluation of depression that identifies the presence and frequency of nine major symptoms of depression in the participant (as recommended by DSM-IV) for two weeks. PHQ-9 is applied frequently in the western world and in sub-Saharan Africa <sup>[35,40]</sup>. Scoring varies from 0 to 27, and the patient who scores ten or more on PHQ-9 is said to be suffering from depression and should be treated for it to avoid severe consequences. Studies provide evidence that PHQ-9 is designed for self-administration, but it gives the same outcomes when the researcher takes interviews based on this questionnaire <sup>[42]</sup>.

### PHQ-2

It consists <sup>13</sup> of the first two questions of PHQ-9 and determines the frequency of low mood, lack of interest, and feeling of happiness for the last two weeks. Questions are valued from 0-3 (4-point scale), where zero represents the complete absence of symptoms and three shows symptoms of depression on each day of the last two weeks with a total score ranging from zero to six <sup>[43]</sup>. A cutoff value of 3 or more indicates the presence of depression and is associated with a high level of sensitivity and specificity for screening depression <sup>[40]</sup>. It is easy to use and can be easily applied by healthcare staff of over-burdened health facilities.

## Data Collection and Study procedures

Prior to the start of data collection, study participants were informed about the study's objective, and verbal informed consent was obtained. The researcher did a face-to-face interview with the PHQ-2 depression screening questionnaire after receiving informed consent. To obtain socio-demographic information, the clinic file of the patient was examined. Due to the low literacy of the study population, the survey was administered by the interviewer, and responses were recorded on paper. Following the screening interview, participants completed the PHQ-9 questionnaire with a second member of the study team who was unaware of the PHQ-2 results. The interview was conducted by local health care practitioners who had been trained in the use of the PHQ-9 questionnaire. The PHQ-9 was given in the same language as the screening interview, with the help of an interpreter if needed. A good sample size of 200 was chosen due to the restricted availability of staff who can diagnose depression. 158 (79%) of the study participants completed the interview. PHQ-2 items were used to calculate total depression screening scores, and the PHQ-9 items were used to calculate total depression diagnosis scores. Patients with a PHQ-9 score of 9 or above are referred to a psychiatrist to confirm the diagnosis of depression.

## Ethical considerations

Ethical approval was obtained from the research ethical review board of the Jinnah hospital Lahore, Pakistan. Before the data collection, informed verbal consent was obtained from each study participant.

## Statistical Analysis

The data analysis was performed using IBM SPSS version 24 software (Chicago, IL) and MedCalc statistical software. Descriptive statistics were used to explain the socio-demographic characteristics of the study participants. To represent continuous data, the mean (standard deviation [SD]) was used, and the two-sample t-test was used to compare groups. Categorical data were assessed using Pearson's  $\chi^2$  test where appropriate. The overall Cronbach's alpha coefficient was used to assess the internal



consistency of PHQ-2 and PHQ-9. Cronbach's alpha was also calculated with each item removed. The criterion validity of PHQ-2 was determined using ROC (receiver operating characteristic) analysis. We used MedCalc 14.8 to analyze the sensitivity, specificity, and positive and negative predictive values of the PHQ-2 as a screening instrument, with the PHQ-9 serving as the reference standard. Statistical significance was evaluated for all tests using a p-value of 0.05. The area under the curve (AUC) determines the performance of a test, and an AUC of 0.5 indicates a non-discriminating test. In contrast, the value of AUC of 1.0 specifies perfect diagnostic accuracy. In sensitivity analyses, cutoffs scores balancing sensitivity and specificity were found out utilizing the point of convergence between sensitivity and specificity and Youden's index, which was calculated by (sensitivity + specificity - 1) [44,45].

## **RESULTS**

### **Participant characteristics**

In total, 158 study participants were completed the PHQ-2 and PHQ-9. The background characteristics of the study participants are mentioned in Table 1. According to the study results, study participants ranged from 18 to 54 years with a mean age of 30.42±7.11years (±SD). One hundred and thirty-five study participants (85.4%) were male, while twenty-three (14.5%) were female. The total score of PHQ-9 ranged from 0 to 22, with the mean PHQ-9 score being 9.92 (SD=4.648). By the present study result, PHQ-9 scores were high between depressed individuals (mean = 12.81) compared to non-depressed individuals (mean = 8.41). In most socio-demographic characteristics, no statistically significant differences were found as evaluated by chi-square and t-test for gender, education, residence, and religion by depression. However, age, marital status, and monthly family income of HIV patients showed a statistically significant difference with the depression (p<0.05).

### **Reliability and item analysis of PHQ-2 and PHQ-9**



The reliability coefficient, Cronbach's alpha for PHQ-9 total score was 0.759, indicating a strong internal consistency. The bivariate correlation between nine items of the PHQ-9 was shown in table 2, with co-efficient ranging from 0.559 to 0.301, and all correlations were statistically significant (all 2-tailed p-values <0.01). Thoughts that you would be better off dead or of hurting yourself and moving and feeling bad about yourself or that you are a failure were the two most frequently endorsed items. On the contrary, Feeling down, depressed, or hopeless was the item least frequently endorsed by HIV patients (Table 2). The PHQ-2 had a Cronbach's alpha of 0.732, indicating that the items of the PHQ-2 were consistent. The corrected inter-total correlation was 0.574 and 0.574, respectively.

### **Sensitivity and specificity for PHQ-2**

Table 3 showed the sensitivity, specificity, predictive values, and Youden's index at different cutoff scores of the PHQ-2 for depression screening. The study results showed that the score of 2 on PHQ-2 indicates the highest Youden's index of 0.924, with a sensitivity and specificity of 0.96. The area under the curve for PHQ-2 was 0.98 (95%CI: 0.953-0.998) (Figure 2), which indicates excellent criterion validity of PHQ-2 in distinguishing between HIV/AIDS patients with and without major depression with a PHQ-9 diagnosis of depression. A PHQ-2 score of 2 was identified as the optimal cutoff for screening of depression (Table 3).

### **Comparison of internal consistency between PHQ-9 and PHQ-2**

According to the present study results, Cronbach's alpha was similar but quite greater for PHQ-9 than in PHQ-2. In ROC curve analysis, The AUC (0.98) was in PHQ-2. The score of 2 on PHQ-2 indicates the highest Youden's index of 0.924, with a sensitivity and specificity of 0.96. When the score of 2 for PHQ2 was assumed, 35.5% of study subjects were diagnosed with probable depression.

## **DISCUSSION**

### **Key findings**

The current study concludes that PHQ-9 and PHQ-2 are useful tools for detecting depression in people affected by HIV living in Lahore, Pakistan. Cronbach's alpha was similar but quite greater for PHQ-9 than in PHQ-2. In ROC curve analysis, The AUC (0.98) was in PHQ-2. The score of 2 on PHQ-2 indicates the highest Youden's index of 0.924, with a sensitivity and specificity of 0.96.

### **Validity and Reliability of PHQ-2 and PHQ-9**

Based on analysis of indicators like Youden's index, sensitivity, specificity, and AUC, a cutoff score of 2 for PHQ-2 was suggested. Anyhow there are a small number of studies assessing the cutoff of depression based on its severity categories [45, 46]. However, there is highly recommended to determine the cutoff scores of depression based on severity categories amid different populations [47, 48]. According to the best of our knowledge, this is the first-ever study on validation and calibration of PHQ-2 in the Lahore, Pakistan. Patel *et al* [16] suggested that the best cutoff score was designed by considering the best balance between sensitivity and PPV and is required for its suitability to person-based location and use. Such an instrument is especially significant for routine application in developing regions where healthcare staff is over-burdened.

The current research showed a cutoff score of 2 while using PHQ-2, sensitivity and specificity were 0.96, but this result was different from already done studies [49-51]. A score of 2 is suggested to suspect a patient is suffering from depression in patients of HIV infection when using the PHQ-2 questionnaire based on current and previous studies. The sensitivity value of our study for PHQ-2 is found to be lower than previous studies when a cutoff value of 3 or more is employed along with a documented reference standard. This result can be clarified because we used a sample of patients enrolled consecutively or by chance. One limitation is the design of the study, which is cross-sectional. For acquiring the required sensitivity, we need longitudinal studies. Enrollment of recently diagnosed HIV patients in our study can make the study prone to bias by increasing the estimation of detection of depression with precision [52].

The internal consistency or alpha coefficient for PHQ-9 was 0.759. The value of Cronbach's alpha must be at least 0.70 or higher for a self-administered questionnaire to

be reliable [53, 54]. The value of the alpha coefficient of PHQ-9 for our study was lesser than previous studies, where its value was 0.79–0.89, respectively [55, 56]. As far as Cronbach's alpha of PHQ-2 is concerned, it is found to be 0.73, which is remarkably good. This value is also in line with the studies done in various populations [49, 57].

### **The prevalence of Depression**

PHQ-2 outcomes showed the frequency of depression to be 35%. This value is higher when compared with previous studies which also used PHQ-2 [48]. This high prevalence of depression in our study participants is consistent across various measures in the results of both instruments, and this concludes that the prevalence of depression in HIV patients in Pakistan can be remarkably higher than the previous estimate. Hence validation with a reliable diagnostic instrument is required to detect the real prevalence of depression [58]. As already discussed in different studies, it is suggested that the first two questions of PHQ-9 may not be able to detect symptoms of depression experienced by HIV patients accurately. It reveals that a remarkable number of HIV patients could not be detected without employing a full PHQ-9 instrument. So it is recommended that PHQ-2 be used for the initial evaluation of patients, but we cannot reach a true conclusion without applying PHQ-9 [58].

### **Strengths and Limitations of the study**

It was the first-ever research done to evaluate the diagnostic accuracy of PHQ-2 for screening major and minor depression in HIV patients by using PHQ-9 as a reference standard. We used a standard instrument that is smaller than other analytical instruments to recognize patients with depression, and it is crucial in primary healthcare settings. PHQ-9 has remarkable properties for the detection of depression and has good capability for assessing the severity of depression.

Especially for evaluation of severity, the PHQ-9 and PHQ-2 offers locally adapted thresholds and follows suggestions to adjust the tool to the background and location when it is intended for application. Because of its shortness, simplicity, and ease of application and interpretation, the use of this instrument is continuously increasing in epidemiological research.

There are a few limitations or constraints in our research. The data were obtained from only one clinic, and hence results cannot be generalized to the population. Because of some reasons, we could not perform test-retest reliability in participants. The study used the cross-sectional design the study, and because of this, we could not establish causation between variables used in our research. Another drawback of this study was that information on participants' mental and physical disabilities was not gathered. <sup>1</sup>Second, we used the PHQ-9 as the reference standard to assess the PHQ-2's sensitivity and specificity as a depression screening instrument. As a result, <sup>1</sup>if the sensitivity or specificity of the PHQ-9 is inadequate, our assessments of the sensitivity and specificity of the PHQ-2 may be biased, and a study using a different diagnostic instrument than the PHQ-9 is recommended. Given that several of the PHQ-9 items were misinterpreted by some participants, we <sup>1</sup>recommend adapting it to the local context and literacy level of the community.

## **CONCLUSION**

HIV patients are more likely than the general population to develop depression. <sup>2</sup>The PHQ-2 and PHQ-9 demonstrated good psychometric qualities, indicating their potential utility as depression screening tools. <sup>1</sup>Given the significant health and social burden of depression and the need for brief, structured, reliable, and valid tools to help healthcare professionals evaluate patients for depression, the PHQ-2 and PHQ-9 would be useful and valuable tools for screening and diagnosing depression in HIV-infected individuals. Moreover, to lessen the global prevalence of psychiatric disorders and improve patient well-being, the instruments can be used in combination with increased access to adequate mental healthcare and therapeutical and non-pharmacological treatments, which are effective in these settings.

## **ARTICLE HIGHLIGHTS**

*Research background*

People living with HIV infection (PLWHA) seem to be more vulnerable to psychiatric morbidity than the overall population, with major depressive disorder seems to be the most prevalent psychiatric diagnosis. Suicidal thinking, anxiety, post-traumatic stress disorder (PTSD), and drug/alcohol use disorders are also frequently documented psychiatric morbidities in HIV patients

### ***Research motivation***

Many HIV-infected patients suffer from depression, but a little focus is given to detecting and treating depression in primary health care. Detection of depression can be improved by introducing short, reliable, and valid screening instruments

### ***Research objectives***

The current study assessed the psychometric properties of the PHQ-2 and PHQ-9 for depression screening and diagnosis and estimated the sensitivity and specificity of the PHQ-2 for depression screening in HIV-infected patients.

### ***Research methods***

A cross-sectional study was conducted on 158 HIV-infected patients aged 18 years and above in Lahore, Pakistan. PHQ-2 was implemented to screen depression. PHQ-9 was implemented to diagnose major depressive disorder (MDD) as a reference standard. Reliability, Validity tests and receiver operating characteristic (ROC) curve were computed.

### ***Research results***

The Cronbach's alpha of PHQ-2 and PHQ-9 were 0.732 and 0.759, respectively. The study results showed that the score of 2 on PHQ-2 indicates the highest Youden's index of 0.924, with both sensitivity and specificity of 0.96, and the area under the curve for PHQ-2 was 0.98 (95%CI: 0.953-0.998).

### *Research conclusions*

<sup>1</sup> Given the significant health and social burden of depression and the need for brief, structured, reliable, and valid tools to help healthcare professionals evaluate patients for depression, the PHQ-2 and PHQ-9 would be useful and valuable tools for screening and diagnosing depression in HIV-infected individuals. Moreover, to lessen the global prevalence of psychiatric disorders and improve patient well-being, the instruments can be used in combination with increased access to adequate mental healthcare and therapeutical and non-pharmacological treatments, which are effective in these settings

### *Research perspectives*

HIV patients are more likely than the general population to develop depression. <sup>1</sup> The PHQ-2 and PHQ-9 demonstrated good psychometric qualities, indicating their potential utility as depression screening tools



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