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Suicide Risk in Persons with HIV/AIDS in South Korea: a Partial Test of the Interpersonal Theory of Suicide

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Abstract

Purpose The high disease burden associated with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) is linked to the elevated suicide risk in this population. Informed by the interpersonal theory of suicide, this study examined how and under which conditions depression is related to suicide risk in people living with HIV/AIDS.

Methods A total of 202 outpatients with HIV/AIDS participated in a cross-sectional and multi-center survey involving four university hospitals in South Korea. This self-reported survey included the Hospital Anxiety and Depression Scale, Interpersonal Needs Questionnaire, and Mini-International Neuropsychiatric Interview suicidality module.

Results Participants' mean age was 48.6 (SD = 13.4) and the majority was male (89.1%). The proportions of those at high, medium, and low suicide risk were 18.5%, 20%, and 15.4%, respectively. Depression was associated with suicide risk directly and indirectly by increasing perceived burdensomeness (PB) and the indirect effect of depression on suicide risk mediated by PB was contingent on the level of thwarted belongingness (TB). PB was associated with suicide risk even after controlling for depression, suggesting its independent effect on suicide risk.

Conclusions PB and TB are potential mechanisms through which depression is associated with suicide risk, supporting the applicability of the interpersonal theory of suicide to understanding a complex interplay of risk factors in people with HIV/AIDS. Moreover, given the independent association of PB with suicide risk, as well as a protective effect of TB in suicide risk, monitoring and management of these factors should be included in the care of people with HIV/AIDS.

Keywords Depression · Human immunodeficiency virus · Perceived burdensomeness · Thwarted belongingness · Suicide

Introduction

As of 2015, 36.7 million persons worldwide were living with human immunodeficiency virus (HIV) [1]. The high disease burden associated with HIV/acquired immunodeficiency syndrome (AIDS) is linked to the elevated suicide risk in this population [2]. Although suicide risk in people living with HIV/AIDS (PLWHA) declined with the introduction of highly

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active antiretroviral therapy (HAART) [3, 4], it remains high compared to the risk in the general population [4]. To illustrate, HIV/AIDS was a significant risk factor for subsequent suicide, with an 8.73-fold higher suicide risk, in a Danish national registry-based study [3]. A systematic review of suicidal behavior related to HIV in 2011 also indicated a high prevalence of suicide in this population, and it was observed that 9.4% of deaths in individuals with HIV were due to suicide as found in autopsy studies, 26.9% of PLWHA reported suicidal ideation, and 22.2% had a suicide plan [5].

Post-HAART studies that examined suicide risk factors in PLWHA observed that an increased suicide risk in this population was related to both young (overall, under 50 years old) [6–8] and old age [4], single status [3], male [4] and female gender [6–8], low income [3] or financial difficulties [6], unemployment [7, 9], and low education [7]. As for clinical factors, a disease stage was not related to suicidal ideation [10], while higher suicide rates in patients with an advanced clinical stage of HIV were observed [4]. Medical comorbidities other than HIV/AIDS [3], a greater number of current AIDS-related conditions [8], or elevated physical symptoms [9] were associated with increased suicide risk, while an increase in CD4 cell counts was associated with a reduced risk [4].

Furthermore, previous studies suggest a significant association between psychiatric disorders and suicide among PLWHA, an association that became stronger after the introduction of HAART. In fact, a study comparing trends and predictors of suicide in HIV-infected individuals pre- and post the introduction of HAART observed that psychiatric comorbidities in suicide cases were more common after than before [4]. Moreover, the interaction of HIV/AIDS with psychiatric illnesses and their comorbidities was associated with increased suicide risk in a Danish national registry study [3]. In particular, the robust association between depression and suicide is consistent throughout studies on PLWHA [7, 11–14]. Major depression was the most prevalent diagnosis among PLWHA with suicidal ideation, with 64% of them having depression [15]. Moreover, depressed PLWHA showed 6.4 times higher odds of lifetime suicidal behavior than their non-depressed counterparts in a study involving 800 people living with HIV in Estonia [13].

Yet, it is necessary to elucidate the mechanisms through which depression is associated with suicide or to consider other factors associated with the heightened suicide risk in PLWHA. The interpersonal theory of suicide (ITS) by Thomas Joiner [16] is a theoretical perspective supported by a decade of empirical research [17] that informs with regard to this issue. The main proposition of the ITS is that "perceived burdensomeness" (PB: the belief that the self is so flawed as to be a liability to others, and self-hatred) and "thwarted belongingness" (TB: "loneliness and the absence of reciprocally caring relationships") are proximal and sufficient predictors of suicidal desire, and the most critical form of suicidal desire is caused by the simultaneous presence of PB and TB [16]. However, individuals are less likely act on that desire unless they have the "acquired capability for suicide," conceptualized as a "lowered fear of death" and "elevated physical pain tolerance" [16].

Previous studies that examined the risk factors for suicide in individuals with physical illness suggested the relevance of the ITS in understanding of suicide risk in PLWHA. Above all, PB has been indicated as an important risk factor for suicide in individuals with physical illness, such as cancer [18, 19] and chronic pain [20, 21]. Few studies have investigated the association between PB and suicide risk in PLWHA.

However, a link between TB and suicide has consistently been observed among PLWHA [22–24]. In fact, a 2003 survey with 2932 French PLWHA found that a lack of social support from the family was independently associated with suicide attempts [6], and the absence of perceived support in relation to HIV status was associated with increased suicide risk among patients visiting a regional reference center for HIV/AIDS treatment in Brazil [7]. Furthermore, owing to the stigma related to their illness, PLWHA tend to conceal their HIV status even from significant others, making them particularly vulnerable to the risk of social isolation or impaired close relationships [25], which in turn may increase suicide risk. For instance, a lack of disclosure of HIV status was related to twofold increased odds of suicidal ideation among 778 patients attending HIV clinics in the UK [9], and social isolation was also related to suicide attempts in a retrospective cohort study with 714 PLWHA from 2000 to 2004 in Puerto Rico [26].

While previous studies have examined various risk factors associated with suicide in PLWHA, most of them are descriptive in nature, exploring these risk factors in isolation, and theory-driven empirical investigations are limited. Moreover, only one study has attempted an empirical investigation of the applicability of the ITS to understanding suicide in PLWHA [27]. This study tested the ITS with 52 individuals attending HIV/AIDS clinics in the USA and found that the suicidal group experienced more PB and feelings of TB compared to the non-suicidal group [27]. However, this study simply compared PB and TB levels by suicidality status (suicidal versus non-suicidal). In doing so, none of the sociodemographic and clinical factors associated with suicide risk in PLWHA, as well as psychiatric comorbidities such as depression, which is a strong suicide risk factor in this population, were taken into account.

Therefore, informed by the ITS, this study aimed to examine how and under which conditions, depression is related to suicide risk in PLWHA. Specifically, we examined whether PB and TB mediate the relationship between depression and suicide risk. The present study also examined whether the effect of depression on suicide risk through PB depends on TB levels, testing the "synergy hypothesis" of the ITS (Fig. 1). The direction of the hypothesis was based on the

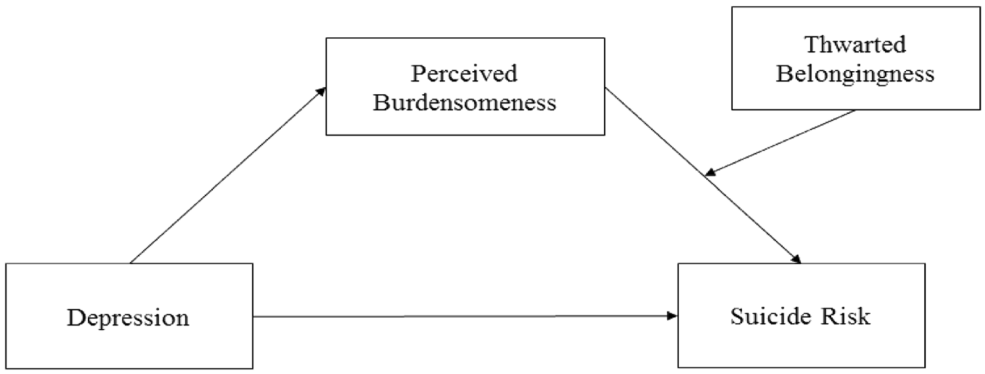

Fig. 1 Hypothesized relationships among study variables

proposition by Van Orden et al.'s [16] review that mental disorders would increase suicide risk through their relationship with PB and TB, as well as on the findings from a prospective study with undergraduate students in the USA, which integrated the ITS into the relationship between depression and suicidal ideation [28], finding that depressive symptoms were associated with an increased sense of TB and PB. These, in turn, were associated with suicidal ideation [28].

Methods

Participants and Procedures

A cross-sectional, multi-center survey involving four university hospitals (two located in Seoul, the capital city, and the other two located in the cities of Seongnam and Busan) in South Korea was implemented from December 2016 to June 2017 using a consecutive sampling procedure. A clinician asked patients who met the inclusion criteria (i.e., being over 18 years of age, being HIV-positive, and being able to read and understand Korean) to participate in the study after their outpatient visit to the clinic. Upon the provision of informed consent, the participants were asked to complete the survey either on site or take it home and return it by mail. A total of 201 patients participated in the study. All participants were rewarded with a gift certificate of value (equivalent to $9). This study was approved by the institutional review boards of the participating institutions. Information regarding participants at a high suicide risk (scores of over 10 on the Mini-International Neuropsychiatric Interview's (MINI) suicidality module) was conveyed to the physician in charge, who was expected to recommend psychiatric consultation and monitor these patients on follow-up visits.

Measures

Depression was assessed by the depression subscale of the Korean version of the Hospital Anxiety and Depression Scale (HADS) [29]. The participants rated each item on a four-point Likert scale (0–3), referring to their experiences in the previous week. The depression subscale (seven items) score ranged from 0 to 21, with a higher score indicating more severe depressive symptoms. Cronbach's α was 0.86 for the depression subscale [29].

PB and *TB* were assessed by the respective subscales of the Korean version of the Interpersonal Needs Questionnaire (INQ) [30, 31]. Participants indicated the degree to which each of the statements was true for them in recent times on a seven-point Likert scale (1 = Not at all true for me, 7 = Very true for me). The INQ has 15 items, divided into two subscales: PB (six items) and TB (nine items). Cronbach's α for the PB and TB subscales was 0.88 and 0.87, respectively.

Suicide risk was evaluated by the Korean version of the MINI suicidality module [32]. The suicidality module is composed of six questions, and each item has a different scoring weight: wish for death (1), wish for self-harm (2), suicidal thoughts (6), suicide plans (10), suicide attempts in the past month (10), and lifetime suicide attempts (4). Three levels of suicide risk can be determined according to the summed score (0–33): low risk, 1–5; medium risk, 6–9; and high risk, over 10.

The self-report survey also included questions regarding sociodemographic characteristics, and participants' clinical characteristics (e.g., CDC disease stage, CD4 cell counts, HIV RNA log) were retrieved from medical records.

Statistical Analyses

Univariate associations of sociodemographic, clinical, and psychosocial variables (i.e., depression, PB, and TB) with suicide risk were examined by the Pearson correlation analysis or analysis of variance (ANOVA). To examine the direct and indirect effects of depression via PB and TB on suicide risk, simple mediation analyses were performed. Subsequently, to examine whether the indirect effect of depression on suicide risk mediated by PB is conditional on TB, a moderated mediation analysis was performed. A significant interaction between PB and TB on suicide risk would indicate moderated mediation. To determine at which level of TB the indirect effect of depression on suicide risk mediated by PB becomes

significant, simple slope analysis and the Johnson-Neyman technique [33] were implemented. A bootstrapping procedure was performed with 5000 iterations. All statistical analyses were performed using SPSS version 21 for Windows and the Hayes PROCESS Macro for SPSS 2.16.2.

Results

Participant Characteristics

Participants' sociodemographic and clinical characteristics are shown in Table 1. The mean age was 48.6 (SD = 13.4). The majority was male (89.1%), not married (74.5%), and educated up to college or higher (44.9%). The participants were well distributed throughout the three stages of HIV as posited by the Centers for Disease Control and Prevention, and the mean years since diagnosis was 8.25 (SD = 5.98).

The proportions of those at high, medium, and low suicide risk were 18.5% (36/195), 20% (39), and 15.4% (30), respectively. Specifically, the rates of wish for death, wish for self-harm, and suicidal thoughts amounted to 34% (67), 15.2% (30), and 38.6% (76), respectively. The rates of suicide plans, suicide attempts, and lifetime suicide attempts were 8.7% (17), 5.1% (10), and 27.4% (54), respectively.

Bivariate Associations Among Sociodemographic, Clinical, and Psychological Factors and Suicide Risk

Correlations among study variables are shown in Table 2. Suicide risk was positively related to depression, PB, and TB. Depression was associated with increased PB and TB. Consistent patterns of negative correlations of depression, PB and TB with employment, monthly income, and insurance status were observed. Moreover, TB was related to age, education, and medical comorbidities. Among the sociodemographic factors associated with suicide risk (i.e., monthly income) and PB (i.e., employment, monthly income, and insurance status), insurance status was highly correlated with monthly income ($r = -0.64$) and employment ($r = -0.58$); therefore, only employment and monthly income were entered as covariates in subsequent mediation analyses. None of the clinical factors were significantly related to suicide risk.

The Roles of PB and TB in the Relationship Between Depression and Suicide Risk: Simple Mediation Analyses

The results of simple mediation analyses examining the roles of PB and TB in the depression-suicide risk relationship are shown in Table 3. Suicide risk was associated with depression ($B = 0.665$), which was positively related to PB ($B = 0.826$).

Table 1 Sociodemographic and clinical characteristics of participants ($N = 202$)

Variables	N (%) or M (SD)
Sociodemographic variables	
Age ($n = 202$)	48.61 (13.41)
20–40	54 (26.7)
41–60	107 (53.0)
> 60	41 (20.3)
Gender ($n = 202$)	
Male	180 (89.1)
Female	22 (10.9)
Education ($n = 198$)	
Less than high school	45 (22.7)
High school	64 (32.3)
College or higher	89 (44.9)
Marital status ($n = 192$)	
Not married (single/divorced/widowed)	143 (74.5)
Married	49 (25.5)
Religion ($n = 195$)	
Yes	106 (54.4)
No	89 (45.9)
Employment status ($n = 191$)	
Employed	95 (49.7)
Unemployed	96 (50.3)
Monthly income ($n = 191$)	
≤ 1 million Korean won (KRW)	66 (34.6)
1–3 million KRW	70 (36.6)
> 3 million KRW	55 (28.8)
Insurance ($n = 169$)	
National health insurance	115 (68.0)
Medical aid	54 (32.0)
Clinical variables	
CDC stage ($n = 195$)	
A (asymptomatic)	67 (34.4)
B (symptomatic)	68 (34.9)
C (AIDS)	60 (30.8)
Years since diagnosis ($n = 162$)	8.26 (5.98)
CD4 cell counts ($n = 199$)	
< 200 cells/ml	9 (4.5)
≥ 200 cells/ml	190 (95.5)
HIV RNA log ($n = 199$)	
Not detected	140 (70.4)
< 40	43 (21.6)
40–2000	9 (4.5)
> 2000	7 (3.5)
ART duration ($n = 188$)	7.17 (5.47)
Psychological comorbidity[a] ($n = 199$)	
Yes	30 (15.1)
No	169 (84.9)
Medical comorbidity[b] ($n = 199$)	
Yes	182 (91.5)

Table 1 (continued)

Variables	*N* (%) or *M* (SD)
No	17 (8.5)
Mode of transmission ($n = 197$)	
Sex with opposite sex	61 (31.0)
Sex with same sex	106 (53.8)
Other	30 (15.2)

[a] Psychological comorbidities: 24 participants had major depressive disorder, 1 had bipolar disorder, 3 had insomnia, 1 had a snoring/sleep apnea problem, and 1 had cognitive dysfunction problems

[b] Medical comorbidities: out of 214 medical comorbidities, there were 50 infectious and parasitic disease (e.g., syphilis-related disease); 17 musculoskeletal and connective tissue diseases (e.g., osteopenia); 8 endocrine system diseases (e.g., hypertriglyceridemia); 22 digestive system diseases; 15 circulatory system diseases; 13 respiratory system diseases; 13 neoplasm diseases; 7 nervous system diseases; 18 skin and subcutaneous tissue diseases; 13 genitourinary system diseases; and 38 others

PB was related to suicide risk even after controlling for depression ($B = 0.223$). Depression was associated with suicide risk after controlling for PB ($B = 0.480$). The indirect effect of depression on suicide risk mediated by PB was significant (the Sobel $z = 2.892$, $p < .01$) and bootstrapping results corroborated the Sobel test (0.036–0.366).

However, the indirect effect of depression on suicide risk mediated by TB was not significant (the Sobel $z = 1.590$, $p = .112$). Depression was positively related to TB ($B = 1.656$), but TB was not related to suicide risk after controlling for depression ($B = 0.086$, $p = .106$).

The Conditional Indirect Effect of Depression on Suicide Risk via PB as a Function of TB: Moderated Mediation Analysis

The results of the moderated mediation analysis are shown in Table 4. The interaction term between PB and TB was significant ($B = 0.014$). The result of simple slope analysis is illustrated in Fig. 2, and the conditional indirect effect of depression mediated by PB was significant only at the level of 1 SD above the mean of the TB score (slope $B = 0.253$). The results of the Johnson-Neyman analysis [33] indicated that depression was significantly associated with suicide risk through PB only in participants with a high TB level (30.8%) (53/172). A significant mediation effect was observed only with a TB score of 37.7 or higher (TB score range 1–63), and the effect of PB on suicide risk increased with increases in the TB score.

Although not significant, the value of TB at 1 SD below the mean coefficient of PB on suicide risk was negative, and the coefficients of PB and TB were negative, suggesting a potential suppressor effect due to high correlations among PB, TB, and suicide risk [34, 35].

Discussion

Based on the ITS, this study investigated the interrelationship of depression, PB, and TB in the context of suicide risk in a multi-center survey involving 202 PLWHA in South Korea.

The proportions of those at high, medium, and low suicide risk were 18.5%, 20%, and 15.4%, respectively, overall comparable to the reported rate (34.1%) among 211 Brazilian people living with HIV in 2014 using the MINI suicidality module [7]. Moreover, 38.6% of the participants had suicidal thoughts, which is within the range of previously reported rates of suicidal ideation in PLWHA, from 31% in 778 outpatients at an HIV clinic in the UK [9] and in 184 men with HIV in China [11] to 44% in 422 HIV-infected Koreans in 2016 [22]. The rates of suicide attempts in the past month and lifetime suicide attempts were 5.7% and 27.4%, respectively, and this lifetime rate is higher than the 13% reported in a prospective cohort study involving 1560 individuals in the USA [14]. Relatedly, 11% of Koreans reported that they had attempted suicide after an HIV diagnosis [22]. All these findings indicate a considerable vulnerability to suicide among PLWHA, requiring its careful monitoring and management.

With regard to the roles of PB and TB in the relationship between depression and suicide risk, the results of simple mediation analyses indicated that depression was directly associated with an increased suicide risk and indirectly associated with increasing PB. PB was associated with suicide risk even after controlling for depression, suggesting an independent effect of PB on suicide risk. A systematic review and meta-analysis testing the ITS found a consistent and robust effect of PB on suicidal ideation [17, 36] and a stronger association of PB with suicidal behavior as compared to TB was observed in the review [17] and in patients with fibromyalgia [37]. Similarly, only PB mediated the association between non-suicidal self-injury history and subsequent suicidal ideation in a prospective study with young adults [38]. A significant role of PB in suicide among individuals with chronic illness, such as chronic pain [20, 21, 39] and cancer [18, 19], has been demonstrated. However, as compared to TB, the construct of PB has not received attention from suicide studies on PLWHA, except one with 52 PLWHA in the USA observing a higher level of PB in suicidal PLWHA [27]. Yet, the current findings suggest that PB appears to be a strong independent indicator of suicide risk among PLWHA. In addition to the first component of PB posited by the ITS (a self-perception of being a burden on others), which is common in the context of chronic illness, self-hatred with its three observable indicators—low self-esteem, self-blame or shame, and a state of agitation [16]—is a salient issue in the context of HIV/AIDS. In fact, self-blame or shame are particularly relevant in PLWHA [40], mainly owing to the stigma related to the illness. For instance, internalized stigma mediated the relationship between perceived community stigma and mental

Table 2 Correlations among study variables

Variables	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Suicide risk																	
2. Depression	0.439**																
3. PB	0.420**	0.501**															
4. TB	0.346**	0.623**	0.520**														
5. Age	−0.053	0.090	0.048	0.149*													
6. Sex	−0.004	−0.037	0.048	−0.016	0.238**												
7. Marital status	−0.127	−0.084	−0.122	−0.121	0.403**	0.052											
8. Education	−0.084	−0.061	−0.031	−0.146*	−0.458**	−0.363**	−0.213**										
9. Religion	0.015	−0.083	0.010	−0.071	0.177*	0.099	0.097	−0.053									
10. Employment	−0.035	−0.220**	−0.284**	−0.237**	−0.222**	−0.149*	0.068	0.260**	−0.117								
11. Income	−0.181*	−0.320**	−0.249**	−0.336**	−0.370**	−0.180*	0.153*	0.467**	−0.053	0.598**							
12. Insurance	0.137	0.281**	0.215**	0.311**	0.248**	0.024	−0.173*	−0.356**	−0.005	−0.583**	−0.644**						
13. CDC stage	0.086	0.019	0.047	0.007	0.146*	−0.067	0.055	−0.113	0.023	0.000	−0.080	0.069					
14. Time since diagnosis	0.101	0.075	−0.032	0.091	0.412**	0.105	0.101	−0.213**	0.056	−0.091	−0.235**	0.246**	0.043				
15. CD4 cell	0.063	−0.063	0.055	0.036	0.046	0.077	−0.017	−0.017	0.013	−0.002	−0.049	0.017	−0.161*	0.153			
16. HIV RNA log	0.066	0.052	−0.007	−0.080	−0.171*	−0.001	−0.015	0.076	−0.070	−0.041	0.156*	−0.116	0.145*	−0.151	−0.337**		
17. ART duration	0.037	0.023	−0.061	0.065	0.417**	0.107	0.151*	−0.232**	0.095	−0.176*	−0.242**	0.254**	0.026	0.954**	0.162*	−0.167*	
18. Medical comorbidity	0.091	0.101	0.094	0.146*	0.219**	−0.122	0.131	0.015	−0.091	−0.041	−0.165*	0.093	0.334**	0.204**	−0.067	−0.024	0.088
M (SD)	5.40 (7.91)	6.87 (4.35)	12.98 (8.70)	33.81 (12.72)	48.61 (13.41)												

Sample size ranges from 136 (insurance, years since diagnosis) to 202 (age, sex); *$p < .05$, **p .01. Age, time since diagnosis, and ART duration are coded as continuous variables

Gender code: 1 = male, 2 = female; marital status code: 0 = not married, 1 = married; education code: 1 = less than high school, 2 = high school, 3 = college or higher

Income code: 1 = (≤ 1 million Korean won (KRW) 2 = (1–3 million KRW) 3 = (> 3 million KRW); insurance code: 1 = National Health Insurance, 2 = medical aid

CDC stage code: 1 = A (asymptomatic) 2 = B (symptomatic), 3 = C (AIDS); CD4 cell counts code: 1 = < 200 cells/ml, 2 = ≥ 200 cells/ml; HIV RNA log code: 1 = Not detected, 2 = < 40, 3 = 40–2000, 4 = 2000; medical comorbidity code: 0 = no, 1 = yes

Table 3 Results for simple mediation model ($N = 176$)

Variables			B^a	SE	t	p
Perceived burdensomeness (PB) as mediator			Direct and total effects			
Depression → suicide risk			0.665	0.128	5.204	< .001
Depression → PB			0.826	0.144	5.745	< .001
PB → suicide risk (controlling for depression)			0.223	0.066	3.397	< .01
Depression → suicide risk (controlling for PB)			0.480	0.135	3.547	< .01
	Value	SE	z	p		
	Indirect effect of depression and significance using normal distribution					
The Sobel	0.185	0.064	2.892	< .01		
	B	SE	LL 95% CI	UL 95% CI		
	Bootstrap results for indirect effect of depression					
Suicide risk	0.185	0.085	0.036	0.366		
Variables			B^a	SE	t	p
Thwarted belongingness (TB) as mediator			Direct and total effects			
Depression → suicide risk			0.743	0.131	5.665	< .001
Depression → TB			1.656	0.189	8.764	< .001
TB → suicide risk (controlling for depression)			0.086	0.053	1.627	.106
Depression → suicide risk (controlling for TB)			0.601	0.157	3.823	< .001
	Value	SE	z	P		
	Indirect effect of depression and significance using normal distribution					
The Sobel	0.142	0.090	1.590	0.112		
	B	SE	LL 95% CI	UL 95% CI		
	Bootstrap results for indirect effect of depression					
Suicide risk	0.142	0.088	− 0.016	0.331		

Model 4 in PROCESS was used to analyze the simple mediation model. Employment and income were entered as covariates

[a] Unstandardized coefficients

LL lower limit, *UL* upper limit, *CI* confidence interval

outcomes, such as self-esteem or self-blame, in 203 people living with HIV in the USA [41], and self-esteem was a major risk factor for suicidal ideation in PLWHA in China [24].

However, the indirect of effect of depression mediated by TB was not significant, nor was the effect of TB on suicide risk controlling for depression. Unlike the consistently observed association between PB and suicidal ideation, TB has not been a significant independent predictor of suicidal ideation in undergraduate students [42, 43], sexual minority adults [44], or in chronic pain patients [45]. The high correlation between PB and TB ($r = 0.52$) might explain a non-significant relationship between TB and suicide in this study. In fact, a community-based cohort study involving 1286 participants in Australia suggested that the effects of TB and PB are not independent, but influence each other reciprocally [46]. In another study with 245 young adults showing a significant level of depressive symptoms, TB mediated the relationship between negative cognitive style and suicidal ideation when TB and PB were examined separately. However, while PB fully mediated the relationship, TB mediated it only partially [47]. Also, a comprehensive systematic review and meta-analysis with research on ITS observed a stronger association between TB and suicidal ideation among older participants [17], suggesting that the relationship might not be pronounced in the relatively younger participants in our study. Furthermore, potential gender-related differences in the association of PB and TB with suicidal ideation were previously observed in an Australian community-based cohort study that found that while PB was related to increased suicidal ideation in both males and females, TB was related to it only in females [46]. The high proportion of males in PLWHA might be another probable reason for the non-significant association between TB and suicide risk in this study.

With regard to the synergy hypothesis, that is, interaction effect between PB and TB in relation to suicide risk, the results indicated that PB mediated the relationship between depression and suicide risk; however, this mediation effect was significant only in individuals with high TB confirming the synergistic effect of PB and TB on suicide risk as posited by the ITS [16, 17, 48]. For instance, the interaction between PB and social support was associated with suicidal ideation in young adults, even accounting for depression [48], and it was a stronger predictor of continuous suicide attempts [17]. The synergy effect was also observed in chronic pain patients, and PB predicted suicidal ideation at high levels of TB, but only marginally at low levels

Table 4 Regression results for conditional indirect effect ($N = 172$)

Predictor	B^a	SE	t	p
Perceived burdensomeness				
Constant	5.905	1.676	3.524	< .01
Depression	0.821	0.145	5.653	< .001
MINI total score				
Constant				
Perceived burdensomeness (PB)	− 0.375	0.214	− 01.752	.082
Thwarted belongingness (TB)	− 0.135	0.076	− 1.778	.077
PB × TB	0.014	0.005	2.925	< .01
Thwarted belongingness	Boot indirect effect	Boot SE	Boot z	Boot p
Conditional indirect effect at TB = $M \pm 1$ SD (simple slope analysis)				
− 1 *SD* (20.47)	− 0.094	0.127	− 0.739	.460
M (33.06)	0.080	0.083	0.956	.340
+ 1 *SD* (45.65)	0.253	0.069	3.652	< .001
Thwarted Belongingness	Boot indirect effect	Boot SE	Boot z	Boot p
Conditional indirect effect at range of values of TB (Johnson-Neyman)				
11.7	− 0.214	0.163	− 01.315	.190
17.1	− 0.140	0.140	− 0.998	.320
22.5	− 0.066	0.119	− 0.554	.581
27.9	0.009	0.099	0.086	.931
33.3	0.083	0.083	1.004	.317
37.7	0.144	0.073	1.974	.050
41.4	0.194	0.069	2.83	< .05
46.8	0.268	0.070	3.820	< .01
52.2	0.343	0.080	4.268	< .01
57.6	0.417	0.096	4.336	< .001
63.0	0.491	0.116	4.253	< .001

Model 14 was used to examine the moderated mediation model. "Range of values" represents an abbreviated version of the output provided by the macro. Employment and income were used as covariate variables

[a] Unstandardized coefficients

[45]. These and the current findings imply that improving TB or social support may alleviate the negative impact of PB on suicide risk in PLWHA. A clinic-affiliated anonymous online support group that fosters a sense of connection and support among participants [49] may be a viable approach for PLHWA to reduce TB and enhance social support.

While the significant association between depression and suicide is well established in PLWHA [11, 50, 51], how and under which conditions depression is related to suicide risk in HIV-infected individuals have not been studied. The current findings suggest that PB and TB are potential mediators underlying the depression-suicide risk relationship in PLWHA, which is partially consistent with the propositions of the ITS. The current results also highlight the fact that PB is a primary risk factor in its own right, while TB might contribute to suicide risk via depression or in association with PB. In fact, while the lack of perceived support regarding HIV status was significant in univariate analysis, it was not so in multivariate analysis, including depression, in 211 Brazilian PLWHA [7]. Related to this, the association between depression and TB observed in this study is in line with previous findings on patients with mental disorders [52] and persons with HIV [15, 23]. Despite the reciprocal nature of the relationship between depression and TB, the current findings concur with previous ones that depression with symptoms that may lead to social withdrawal [52] is related to TB. Depression may exacerbate a sense of TB among PLWHA, who are already carrying a considerable disease burden in terms of social relationships owing to illness-related stigma. This is because depression can heighten sensitivity to social rejection [53], which warrants the need for integrating its screening and treatment into routine HIV/AIDS care.

Among sociodemographic factors, only income was significantly correlated with suicide risk [3], while none of the clinical characteristics were associated with it. Although some previous studies with PLWHA found associations between suicide and clinical factors, such as medical comorbidities

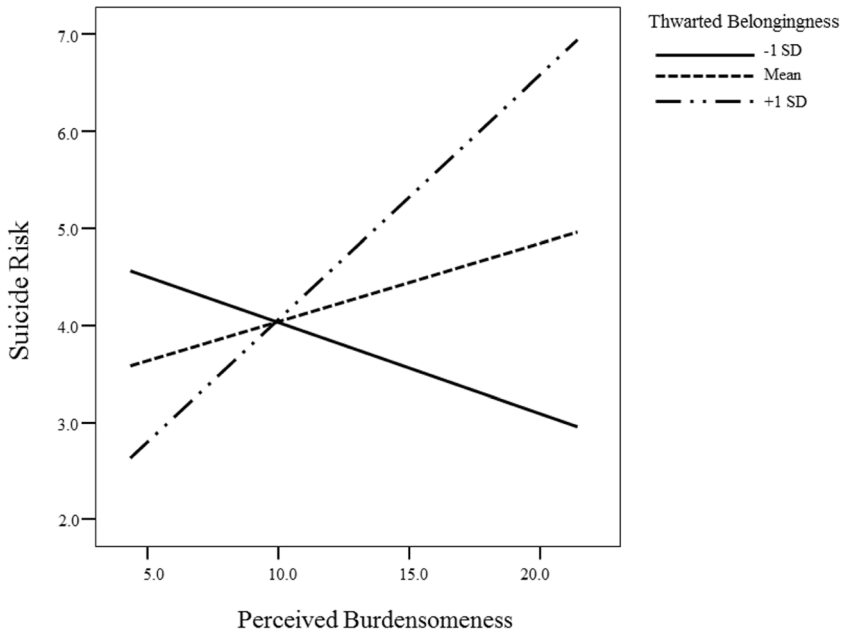

Fig. 2 The conditional indirect effect of depression on suicide risk via PB as a function of TB

[3], HIV symptom severity [12], or CD4 cell counts [4], a prior study conducted in the pre-HAART period (between 1989 and 1992) involving 164 HIV-positive men in Australia suggested that disease severity indices, such as the number of physical HIV symptoms or disease stage, had far less influence on suicide attempts in these individuals than psychiatric comorbidities, particularly depression and psychological adaptation [54]. Relatedly, a comparison of suicide trends in a Swiss HIV cohort noted an increased role of mental illness in suicide over disease-related factors in the HAART period compared to the period before its introduction [4]. Moreover, a study with 422 Korean PLWHA found that the impact of psychological factors, such as treatment history for depression, appears to be greater than that of AIDS-defining opportunistic diseases (adjusted odds ratio of 6.11 versus 2.08, respectively) on suicidal ideation, and none of the clinical factors were associated with suicide attempts in multivariate analysis. However, in the present study, the potential associations of clinical factors with suicide risk may have been undetected or underestimated owing to the relatively small sample size and overall good level of HIV-related condition of participants, with 95.5% having CD4 cell counts of ≥ 200 cells/ml and 92% with an HIV RNA log value less than 40, warranting cautious interpretation regarding the association between clinical factors and suicide risk.

Of note, depression, PB, and TB, which were associated with suicide risk in the present study, showed significant associations with employment, income, and health insurance status. While previous studies suggest a significant association of employment status [7, 9, 26] and national medical aid beneficiary status [22] with suicide risk among PLWHA, these associations might in part be due to their link with depression, PB, or TB. As health insurance and employment status were highly correlated with income (r = 0.598, −0.583) and income was correlated with suicide risk, income appears to be a stronger factor in suicide risk among PLWHA, indicating the need for suicide prevention efforts to include the monitoring of economically disadvantaged PLWHA.

However, employment status should be considered beyond its association with income. Work is not just a source of income but also of self-worth or meaning [55], and being unable to work might lead to the loss of an important source of meaning [55], increasing the suicide vulnerability factors of PB. In fact, unemployment is a factor that increases the perception of being a burden on others [16]. Moreover, unemployment is associated with loss of social support or diminished or disrupted social or family relationships [56], which may lead to loneliness, a major predictor of suicide risk in 2973 people receiving HIV care in France [57]. Given the association of employment status with both depression and suicidal ideation among PLWHA [23], it should be addressed in the management of suicide risk in this population.

The findings from the present study should be interpreted within their limitations. Above all, the cross-sectional design does not allow for causal interpretations of the proposed relationships among study variables, such as depression, PB, and TB, in their relationship with suicide risk. For instance, a bidirectional relationship between depression, PB, and TB is possible, and a prospective longitudinal study can inform about a temporal relationship between these variables. The use of self-report measures to assess depression or suicide risk might be another limitation leading to social desirability bias, and assessment of these variables by implicit measurement, as

well as PB by behavioral tasks, is suggested [17]. Moreover, owing to consecutive sampling procedures, the possibility of sampling bias cannot be excluded, limiting generalizability of the findings to all PLWHA. Patients with poorer physical or psychological functioning were less likely to participate in the study, resulting in an underrepresentation of more vulnerable participants and, thus, underestimation of the studied variables. Furthermore, acquired capability, the third main construct of the ITS, and hopelessness, conceived as the perceived intractability of PB and TB [17], were not included in this study, and additional research including these constructs is warranted to test the ITS in its complete form.

Despite these limitations, to the best of our knowledge, this is one of the first studies to examine the applicability of the ITS in elucidating the complex interplay of factors involved in suicide risk among PLWHA. The fact that 38.5% of the participants were at moderate to high suicide risk underscores the need to monitor suicide risk in this population. Previous findings suggest that the monitoring of psychiatric morbidities or suicide risk should be initiated with the diagnosis of HIV/AIDS. For instance, a Danish national registry study found that psychiatric illness developed after the diagnosis of HIV/AIDS in 94.4% of those who died from suicide and 90.6% of controls [3]. Suicide risk was also heightened in the early period after an HIV/AIDS diagnosis [3, 11, 58], with 42% of attempted suicides occurring within the first month and 27% within the first week [58]. However, routine screening for suicide risk or depression might be not feasible in many HIV/AIDS care facilities. The implementation of a routine, self-administered computerized screening system for suicidal ideation and associated conditions, as well as an automated notification of risk to the treatment team, has proved a practical approach allowing for timely detection and intervention for suicide risk in HIV clinics [50].

Furthermore, given their significant roles in suicide risk among PLWHA, monitoring for PB and TB is warranted. Stellrecht et al. [59] suggested that inquiring about one's ability for self-care in various aspects of life (for PB), and the number and quality of interpersonal relationships as well as perceived level and meaning of social involvement (for TB), is a viable way to assess these related concepts. Furthermore, as PB and TB might be misperceptions stemming from a cognitive distortion of one's significance to others and their integration with one's social network [59], a cognitive behavioral approach can be an effective treatment option and was also proven to be an efficacious approach for HIV-infected individuals with depression [60, 61]. For the management of PB and TB to be effective, the cultural context of South Korea should be taken into consideration. Stigma and its psychological implications, such as shame, may be particularly salient in Korea owing to a "face-saving culture" with its emphasis on maintaining honor [62]. Having a family member with a stigmatized disease like HIV/AIDS can threaten the family honor, inflicting a considerable sense of shame and distress on the entire family. The family member with HIV/AIDS may feel shame or guilt, exacerbating the sense of being a burden on the family, and other family members can be less supportive toward the member responsible for family dishonor, which may worsen the sense of TB in this family member. In view of this, family-based supportive interventions may be helpful. For instance, a psychosocial support group for HIV-affected families in Haiti improved psychosocial functioning in youths with HIV and depressive symptoms and HIV-related stigma in their caregivers [63]. Moreover, family nursing interventions delivered by a family nurse with 16 Thai families promoted competence in caring for a family member with HIV/AIDS and improved family interactions [64].

To conclude, the results suggest that PB and TB are potential mechanisms underlying the depression-suicide relationship, providing initial support for the relevance of the ITS as a theoretical framework elucidating the complex interplay of significant suicide risk factors in PLWHA.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This study was approved by the respective Institutional Review Boards of the participating institutions.

Informed Consent We obtained the informed consent from the participants.

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