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ORIGINAL PAPER

Association between perinatal depressive symptoms and suicidal risk among low-income South African women: a longitudinal study

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Abstract

Purpose The aim of this study was to assess the association between depressive symptoms and suicidal risk over time among perinatal women at risk for depression antenatally, and assess modifying effects of age, perinatal stage and depressive symptom trajectory.

Methods A total of 384 adult pregnant women were recruited from two antenatal clinics in an informal settlement near Cape Town, South Africa, and followed up at eight months gestation, and at 3- and 12-month postpartum. The MINI 6.0 Suicidality module and the Hamilton Depression Rating Scale (HDRS) were used to measure suicidal risk and depression, respectively. Generalised Estimating Equations were used to assess the association between change in depressive symptoms from one assessment to the next (predictor) and change in suicide score or change in suicidal risk (score ≥ 9) (outcomes).

Results HDRS scores were positively correlated with suicide score (95% CI 0.35, 0.78; $p < 0.001$), and with odds of being at moderate risk for suicide, after controlling for risk of suicide at the previous assessment (adjusted odds ratio = 1.15; 95% CI 1.09, 1.22; $p < 0.001$). Age was a significant effect modifier: change in HDRS scores was not associated with change in suicide scores among participants aged 35–45 years. Secondary analyses indicated that a decrease in HDRS score was associated with a decrease in suicide scores, but an increase in HDRS score was not associated with change in suicide score.

Conclusions Depression and suicide are overlapping but relatively independent phenomena, especially among older or more chronically depressed perinatal women.

Keywords Suicide · Depression · Perinatal · Longitudinal · South Africa

Introduction

Suicide was recently estimated the 18th leading cause of death globally [1]. Contrary to high-income countries (HIC), where the risk of suicide increases with age [2], suicide in low- and middle-income countries (LMICs) is the leading cause of death among 15–29 years old [1]. It is also the leading cause among women aged 15–19 years [3], ahead of maternal mortality. In South Africa, 1% of maternal deaths were due to suicide between 2014 and 2016 [4], while the prevalence of suicidal ideation ranges between 14 and 28% among perinatal women [5–7].

Globally, rates of suicide are usually lower among the perinatal population compared to the general population [5], thought to be because women who get pregnant are usually healthier [8], or because of women's concern for the fetus and increased social support and contact with health services during pregnancy [5]. This may be less applicable in LMICs, however, where pregnancies are more likely to occur

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in the context of HIV, poverty, substance use, interpersonal violence, and lack of partner support [9–12]—all of which have been shown to increase the risk of suicide in LMICs [2, 13, 14] and South Africa more specifically [6, 15]. These have also been identified as risk factors for perinatal depression, which is estimated to affect 13% of women in LMICs [16]. In South Africa, the prevalence of antenatal and postnatal depression recorded has been as high as 47% and 35%, respectively [17, 18].

Unsurprisingly, depression and suicidal behaviors (ideation, plan, or attempt) are strongly associated. Globally, approximately 90% of individuals who commit suicide suffer from a mental disorder [19], and half of these suffer from depression or a mood disorder [2, 20]. In South Africa, results from the South African Stress and Health (SASH) study, a 2002 survey among a representative sample of South African adults, indicated that 24% and 27% of individual reporting lifetime suicidal ideation and attempts, respectively, had a history of major depression [21]. Similar associations between depression and suicidal ideation have been reported among perinatal women in South Africa [6, 7, 15]. However, Onah et al. [7] found that a diagnosis of mood disorder among pregnant women, whilst associated with suicidal ideation, was not associated with suicide plan or attempt. In addition, in the same study, more than half of women who reported suicidal behavior did not suffer from depression, anxiety, or personality disorder. This mirrors findings reported among the general population in South Africa [21] and other LMICs [22], suggesting that depression and suicidal risk may be overlapping but separate entities [5].

Latent modelling techniques have shown that trajectories of perinatal depressive symptoms are heterogeneous [23, 24]. Studies in South Africa have shown that women report relatively chronic trajectories, while others show a natural remission over the perinatal period [25, 26]. Recent research has also conceptualized suicidal risk as cyclical or episodic [13], and this had led to several studies investigating its longitudinal patterns [27–29]. Using similar latent suicidal risk techniques, evidence also suggests different courses of suicidal risk over the lifetime [29, 30]. While these methods have not been used to assess the association between depression and suicidal behaviors over time, there is emerging evidence that the course of suicidal risk may be associated with the course of depression [31–33].

To the best of our knowledge, the longitudinal investigation of depression in relation to suicidal risk has not been conducted among perinatal women in LMICs. So far, all studies on depression and suicidal risk among perinatal women in South Africa have been cross-sectional [6, 7, 15, 18]. While these have been useful in identifying at-risk groups, longitudinal studies would be helpful in understanding the relationship between depression and suicidal behaviors over time, especially given the heterogeneous trajectories of depressive symptoms. This would, indeed, have direct implications on the treatment and follow-up of perinatal women presenting with either depressive symptoms. The present paper tries to address this gap by investigating the longitudinal association between depressive symptoms and suicidal risk among perinatal women living in a low-resource setting in South Africa, who are at risk for depression during pregnancy. The objectives of the study were to identify whether change in depressive symptom severity was associated with change in suicidal risk over time, and whether this association varied depending on age, stage in the perinatal stage, and depressive symptom trajectory.

Methods

Design

This study is a secondary analysis of data collected for an individual randomized-controlled trial (RCT) among pregnant women living in Khayelitsha, a peri-urban informal settlement near Cape Town, South Africa. The RCT's objective was to assess the effectiveness of a six-session task-shared psychological intervention, delivered by community health workers (CHW), to treat perinatal depressive symptoms. No significant differences in depressive symptoms or suicidal risk were found over time [34], so both arms were combined into one sample for the purpose of the present study. The RCT methods were described previously [35], and are briefly summarized here.

Participants

Pregnant women were approached during their first antenatal visit in one of two antenatal clinics in Khayelitsha. Participants recruited into the RCT were 18 years or older, not more than 28 weeks pregnant, spoke isiXhosa, lived in Khayelitsha, and scored 13 or above on the Edinburgh Postnatal Depression Scale (EPDS; [36]). The EPDS has been validated among isiXhosa-speaking women in South Africa, and a cut-off of 13 suggests high risk for depression [37, 38]. A total of 425 participants were enrolled into the RCT from October 2013 to October 2014. Six participants were wrongly enrolled as they did not meet the inclusion criteria (not pregnant or not isiXhosa-speaking), and 41 participants reported a pregnancy or baby loss during the study—these participants were excluded from the present analysis. The final sample, therefore, consisted of 384 participants.

Procedure

Once enrolled, participants were randomized into the psychological treatment or enhanced usual care (3-monthly phone calls). All participants received the same routine antenatal care at the clinics. The baseline assessment was conducted at the clinic on the day of recruitment, and participants were followed up at 8-month gestation, and again at 3-month and 12-month postpartum. All assessments were conducted by trained fieldworkers who were blind to the participants' allocation arm. Follow-up assessments were conducted at home or at the clinic, depending on the participants' preference. Data were collected using mobile devices (www.mobenzi.com).

Instruments

The assessment instruments were translated to isiXhosa and back-translated into English by two independent translators. Participants' demographic and socio-economic characteristics were collected during the baseline assessment, including age, highest education level, as well as employment, partner status, and HIV status. Each assessment also included a range of measures covering social- and health-related measures. Only those pertaining to the present study are presented here.

Suicidal ideation and behaviors

The Mini-International Neuropsychiatric Interview (MINI) 6.0 [34] Suicidality module was used to assess suicidal behaviors in the past month. The module is a structured diagnostic interview comprising 13 questions covering a range of suicidal behaviors, including ideation and self-harm. Scores range from 0 to 76; greater scores suggest greater suicidal risk. According to the MINI guidelines, a score of 9–16 suggests a moderate risk of suicide, while a score of 17 or more suggests high risk [39]. For the purpose of this study, the main outcome was a score of 9 or above, denoting moderate suicidal risk. Participants' responses to the items relating to the presence of ideation, plans, or attempts in the past month were also noted. The MINI 6.0 has been used across many different settings and populations, including among postnatal women from Khayelitsha [15] and among pregnant women from another informal settlement near Cape Town [7].

Depressive symptoms

Depressive symptoms were assessed using a revised version of the Hamilton Depression Rating Scale (HDRS) [40], adapted for use by trained fieldworkers for the RCT specifically. The HDRS is a 17-item rating scale assessing symptoms in the past 2 weeks; greater scores suggest greater symptom severity. The revised version of the HDRS has been validated in this population [41], and shows adequate test–retest validity. To avoid circularity [31, 32], the suicide item was excluded from the HDRS total score in the present study—the maximum score was, therefore, 50. The internal consistency of the 16-item HDRS, measured using Cronbach's Alpha (α), was acceptable across timepoints ($\alpha = 0.67$–0.79).

The MINI 6.0 Major Depression Episode module, also based on the DSM-IV criteria, was also administered to identify women with a current diagnosis of major depression.

Statistical analysis

Analyses were conducted in Stata version 14 [42]. Baseline demographic and socio-economic characteristics of the sample, as well as suicide- and depression-related measures over time were investigated using measures of central tendency [means and standard deviations (SD)] for continuous variables, and frequencies and percentages for categorical variables. Differences in baseline characteristics between participants with full and partial data were assessed using the non-parametric Fisher's exact test for categorical variables and Wilcoxon rank-sum test for continuous variables.

Generalized Estimating Equations (GEE) were used to assess the association between depressive symptoms (predictor) and suicidal risk (outcome) over time. This method of analysis was chosen as it adjusts standard errors for the correlation between multiple observations for each participant. Two different suicidal risk outcomes were assessed: risk of suicide (score ≥ 9) and change in suicide score (change in severity of suicidal risk) from one assessment to the next. The latter was calculated for each participant by subtracting from the suicide score at each time point the suicide score from the previous assessment. A negative change or positive change in suicide score from one assessment to the next, therefore, meant a decrease or increase in score, respectively.

The relation between change in HDRS score and change in suicide score was assessed in a series of four models. All models were adjusted for age of participant at baseline (< 25 years, 25–34 years, or ≥ 35 years) and for 'trajectory group'. The latter variable categorized women into two latent groups, depending on the trajectory of their depressive symptoms over the perinatal period, identified in a previous study among the same sample using growth mixture modelling [25]: an 'antenatal only' trajectory, with mild-to-moderate symptoms at recruitment, which decreased steadily from pregnancy to 12-month postpartum; and an 'antenatal and postnatal' trajectory, characterized by moderate-to-severe symptoms, which decreased temporarily from pregnancy to 3-month postpartum, but increased again at 12-month postpartum. In the same study, the two

trajectories showed different patterns of socio-demographic and clinical risk, including suicidal risk, thus justifying the inclusion of the variable among the possible confounders. The first of the four models included individual change in HDRS score as a predictor, which was calculated in the same way as change in suicide score. The second, third, and fourth models also included the interaction of change in HDRS score with participant age at baseline (< 25 years, 25–34 years, or ≥ 35 years), perinatal stage (pregnancy or postnatal period), and trajectory group ('antenatal only' or 'antenatal and postnatal'), respectively.

Another series of four models were fitted with the same predictors but with suicidal risk (score ≥ 9) as outcome. In addition to adjustments for age and trajectory group, the four models were adjusted for risk of suicide at the previous assessment. This way, each model assessed change in HDRS score from one assessment to the next in predicting risk of suicide at the next assessment above and beyond the risk of suicide at the previous assessment.

Secondary analyses were conducted to assess whether the association between HDRS and suicide scores varied depending on the direction of the change in HDRS scores. The same four models were computed again with change in suicide score as the outcome, this time adding a binary variable (decrease vs increase in HDRS score since the previous assessment) as an interaction term with change in HDRS score. This way, two coefficients of unit change in suicide score would be generated per model: one for a one-unit change decrease in HDRS score and one for a one-unit increase in HDRS score.

An investigation into the correlation of change in suicide scores and suicidal risk over time suggested a different and random correlation pattern across timepoints, so an unstructured working correlation matrix was assumed and included as a covariate in all models. However, a robust variance estimator was used to adjust standard errors in case where the correlation matrix was not applicable. Analyses were based on observed data and assumed that data were missing completely at random. Dang et al. [43] reviewed power and sample size calculations for GEE models, and given an attrition ranging between 12 and 24% over the three follow-up assessments and an unstructured within-subject correlation, the sample size of 384 participants was considered sufficient to achieve 80% power.

Ethics

Participants who scored 17 or above the MINI Suicidality module during data collection were automatically identified as being at high suicidal risk and were immediately referred to a psychiatric nurse in an adjacent community health center. This study was approved by the University of Cape Town (UCT)'s Human Research Ethics Committee (HREC REF 835/2015). The original RCT also received ethics approval from UCT (HREC REF 226/2011).

Results

Sample characteristics

The baseline socio-demographic characteristics of participants included in the study are presented in Table 1. Participants were, on average, 27 years old (SD = 5.62) and in their 18th week of pregnancy (mean = 17.2; SD = 5.71; median = 18, interquartile range = 14–22). The majority of participants had not completed high school (n = 225, 58.6%), were unemployed (n = 207, 53.9%) and did not live with their partners (n = 254, 66.1%). Nearly a third were HIV-positive (n = 112, 30.1%).

On average, participants were followed-up for their 8-month assessment 17.2 weeks (SD = 5.9; Median = 18; IQR = 12–20) after their baseline assessment. Of the 384 participants included in this study, 252 participants (65.6%) had complete data at all four timepoints, and 27 (7.0%) participants completed the baseline assessment only. Participants aged between 18 and 24 years were more likely to have incomplete data (at least one assessment missed) (n = 61, 45.5%) compared to participants aged at least 25 years (n = 71, 28.4%) (χ^2 = 11.3, p = 0.001). Unemployed participants (n = 81, 39.1%) were also more likely to have missed at least one assessment compared to employed participants (n = 51, 28.8%) (χ^2 = 4.5, p = 0.034).

At baseline, 87 (22.7%) participants scored at or above the moderate risk threshold on the MINI suicidality module; 76 reported suicidal ideation (19.8%) and 64 (16.7%) reported having made suicide plans in the past month (Table 2). In addition, 3.4% (n = 13) of participants reported having made a suicide attempt in the past month. Among those who were at risk for suicide at baseline (n = 87, 22.7%), 59.7% (n = 52) reported moderate or severe depressive symptoms on the HDRS and 71.3% (n = 62) were diagnosed with depression on the MINI. However, among those diagnosed with depression (n = 157, 40.9%), only 39.5% (n = 62) were at risk of suicide. The proportion of participants at risk of suicide and reporting suicidal behaviors decreased steadily over the course of the study. The average HDRS scores and proportion of participants diagnosed with depression also decreased from recruitment to 8-month gestation but remained relatively stable over the remainder of the postnatal period.

The results of the GEE predicting change in suicide scores and risk of suicide are presented in Tables 3 and 4. After controlling for age and trajectory group, change in HDRS scores was associated with both suicide outcomes: a one-point unit change in HDRS score from one assessment

Table 1 Baseline characteristics of the sample

	Mean	SD
Gestation (weeks)	17.2	5.71
Age (years)	27.2	5.62
	n	%
Age group		
18–24 years	134	34.9
25–34 years	204	53.1
35–45 years	46	12.0
Education level		
Less than high school completed	225	58.6
Completed high school or higher	159	41.4
Employment status		
Employed	177	46.1
Not employed	207	53.9
Partner status		
Lives with partner	130	33.9
Does not live with partner	254	66.1
HIV status ($n=372$)		
Negative	260	69.9
Positive	112	30.1

SD standard deviation

Table 2 Descriptive statistics for depression and suicide outcomes over time

	Baseline ($n=384$)		8-month gestation ($n=290$)		3-month postpartum ($n=337$)		12-month postpartum ($n=320$)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
HDRS score	15.2	4.44	12.6	4.80	9.6	4.66	10.1	4.65
Suicide score	7.8	15.4	3.2	9.02	2.1	7.39	1.7	6.23
	n	%	*n*	%	*n*	%	*n*	%
Diagnosis of depression	157	40.9	67	23.1	58	17.2	74	23.1
Moderate/high suicide risk[a]	87	22.7	28	9.7	14	4.2	9	2.8
Suicidal ideation	76	19.8	28	9.7	12	3.6	8	2.5
Suicide plans	64	16.7	18	6.2	10	3.0	8	2.5
Suicide attempt	13	3.4	3	1.0	2	0.6	1	0.3

SD standard deviation

[a]Defined as a score of 9 or more (MINI 6.0 suicidality module)

to the next was associated with a 0.57 point unit change in suicide score (95% CI 0.35, 0.78; $p<0.001$); it was also associated with greater odds of being at moderate risk for suicide [adjusted odds ratio (aOR) = 1.15; 95% CI 1.09, 1.22; $p<0.001$] after controlling for risk of suicide at the previous assessment.

The effect of age, perinatal stage, and trajectory group on the association between individual change in HDRS score and individual change in suicide scores are presented in Fig. 1. Age was a significant effect modifier: a one-point unit change in HDRS score was associated with a 0.68-point (95% CI 0.38, 0.98; $p<0.01$) and a 0.60-point (95% CI 0.27, 0.92; $p<0.001$) unit change in suicide score among the younger (18–24 years old) and the middle-age participants (25–34 years), respectively. However, change in HDRS scores was not associated with change in suicide scores among the older group (35–45 years old) [adjusted (a) $\beta=0.16$; 95% CI − 0.26; 0.55; $p>0.05$]; the difference

Table 3 Generalised Estimation Equations predicting change in suicide score from change in HDRS score, age, perinatal stage, and depressive symptom trajectories groups

Predictors	Model 1 (change)		Model 2 (change × age)		Model 3 (change × perinatal stage)		Model 4 (change × trajectory)	
	aβ[a] (SE)	95% CI	aβ[a] (SE)	95% CI	aβ[a] (SE)	95% CI	aβ[a] (SE)	95% CI
Change in HDRS score	**0.57 (0.11)**	**0.35; 0.78*** **	0.68 (0.15)	0.38; 0.98***	0.63 (0.23)	0.17; 1.09**	0.50 (0.12)	0.27; 0.73***
Age								
18–24	Ref	–	Ref	–	Ref	–	Ref	–
25–34	0.72 (0.72)	−0.68; 2.13	0.55 (0.68)	−0.80; 1.89	0.69 (0.72)	−0.73; 2.11	0.73 (0.71)	−0.67; 2.13
35–45	2.34 (1.01)	0.72; 3.96**	1.43 (0.98)	−0.50; 3.35	2.30 (0.83)	0.67; 3.93**	2.38 (0.83)	0.75; 4.01**
Trajectory								
Antenatal only	Ref	–	Ref	–	Ref	–	Ref	–
Antenatal and postnatal	−0.86 (1.15)	−3.12; 1.40	−0.89 (1.16)	−3.16; 1.37	−0.67 (1.14)	−2.91; 1.56	−0.36 (1.13)	−2.57; 1.85
Perinatal stage								
Pregnancy	–	–	–	–	Ref	–	–	–
Postpartum	–	–	–	–	2.26 (1.15)	−0.01; 4.52	–	–
Change × age								
18–24	–	–	**Ref**		–	–	–	–
25–34	–	–	**−0.08 (0.22)**	**−0.52; 0.36**	–	–	–	–
35–45	–	–	**−0.53 (0.26)**	**−1.04; −0.03***	–	–	–	–
Change × perinatal stage								
Pregnancy	–	–	–	–	**Ref**		–	–
Postpartum	–	–	–	–	**−0.16 (0.23)**	**−0.62; 0.30**	–	–
Change × trajectory								
Antenatal only	–	–	–	–	–	–	**Ref**	**–**
Antenatal and postnatal	–	–	–	–	–	–	**0.38 (0.33)**	**−0.26; 1.02**

CI confidence intervals, *HDRS* Hamilton Depression Rating Scale, *SE* standard error

*$p<0.05$; **$p<0.01$; ***$p<0.001$

[a]Coefficients represent the change in suicide score per unit change in HDRS score; coefficients of interests are in bold

in slope between the older and younger groups was significant (a$\beta=-0.53$, 95% CI −1.04, −0.03; $p<0.05$). A similar trend was noted when assessing risk of suicide: the odds of being at risk for suicide were 1.17 times greater with every one-point increase in HDRS score, both among the younger group (95% CI 1.07, 1.27 $p<0.01$) and among the middle-age participants (95% CI 1.08, 1.26; $p<0.001$). No association was found among the older group (aOR 1.04; 95% CI 0.85, 1.27; $p>0.05$). The difference in odds across age groups failed to reach statistical significance, however.

There was no effect of perinatal stage on the association between change in HDRS scores and change in suicide scores (a$\beta=0.16$; 95% CI −0.62; 0.30; $p>0.05$) or suicidal risk (aOR 0.93; 95% CI 0.83; 1.05; $p>0.05$). There was also no effect of the trajectory group on the association between change in HDRS scores and change in suicide score (a$\beta=0.38$; 95% CI −0.26; 1.02; $p>0.05$), but there was an effect of trajectory group on the association between change in HDRS scores and suicidal risk (aOR 0.91; 95% CI 0.82; 1.00; $p<0.05$): the odds of being at risk of suicide with a one-unit change in HDRS score were greater among the 'antenatal only' trajectory group (aOR 1.19; 95% CI 1.10; 1.29; $p<0.001$) compared to the 'antenatal and postnatal' trajectory group (aOR 1.08; 95% CI 1.02; 1.15; $p<0.01$).

The secondary analyses indicated that a one-unit decrease in HDRS score was associated with a −0.72 unit decrease in suicide scores (95% CI −0.31; −1.14; $p<0.01$), but a one-unit increase in HDRS score was not associated with change in suicide score (a$\beta=0.24$; 95% CI −0.30; 0.79; $p>0.05$). Neither age, time in the perinatal stage, nor trajectory group had an effect on these associations, however. Interestingly, while a one-unit decrease in HDRS score was associated with a 0.59 (95% CI 0.06; 1.11; $p<0.05$) and 0.84 (95% CI 0.23; 1.45; $p<0.01$) unit decrease in suicide score among younger and middle-age participants, respectively, this was not associated with a decrease in suicide score among the

Table 4 Generalised Estimation Equations predicting suicide risk from change in HDRS score, age, perinatal stage, and depressive symptom trajectories groups

Predictors	Model 1 (change)		Model 2 (change × age)		Model 3 (change × perinatal stage)		Model 4 (change × trajectory)	
	aOR (SE)	95% CI	aOR (SE)	95% CI	aOR (SE)	95% CI	aOR (SE)	95% CI
Change in HDRS score	**1.15 (0.03)**	**1.09; 1.22*****	1.17 (0.05)	1.07; 1.27**	1.21 (0.05)	1.10; 1.32***	1.19 (0.05)	1.10; 1.29***
Age								
18–24	Ref	–	Ref	–	Ref	–	Ref	–
25–34	0.79 (0.25)	0.42; 1.49	0.80 (0.26)	0.42; 1.50	0.67 (0.23)	0.34; 1.33	0.80 (0.25)	0.43; 1.49
35–45	0.58 (0.38)	0.16; 2.11	0.69 (0.43)	0.20; 2.31	0.54 (0.37)	0.14; 2.07	0.61 (0.39)	0.17; 2.14
Trajectory								
Antenatal only	Ref	–	Ref	–	Ref		Ref	
Antenatal and postnatal	2.53 (1.14)	1.05; 6.13*	2.60	1.08; 6.25*	3.75 (1.83)	1.44; 9.76**	2.83 (1.14)	1.28; 6.24*
Suicide risk (previous assessment)								
Low	Ref	–	Ref	–	Ref	–	Ref	
High	10.47 (3.45)	5.48; 19.99***	11.19 (3.60)	5.95; 21.03***	5.58 (2.08)	2.68; 11.59***	10.08 (3.36)	5.25; 19.36***
Perinatal stage								
Pregnancy	–	–	–	–	Ref		–	–
Postpartum	–	–	–	–	0.28 (0.10)	0.14; 0.54***	–	–
Change × age								
18–24	–	–	**Ref**	**–**	–	–	–	–
25–34	–	–	**1.00 (0.06)**	**0.89; 1.13**	–	–	–	–
35–45	–	–	**0.89 (0.10)**	**0.72; 1.11**	–	–	–	–
Change × perinatal stage								
Pregnancy	–	–	–	–	**Ref**	–	–	–
Postpartum	–	–	–	–	**0.93 (0.06)**	**0.83; 1.05**	–	–
Change × trajectory								
Antenatal only	–	–	–	–	–	–	**Ref**	–
Antenatal and postnatal	–	–	–	–	–	–	**0.91 (0.04)**	**0.82; 1.00 ***

Adjusted odds ratios represent the odds of being at risk of suicide for every unit change in HDRS score; coefficients of interests are in bold

aOR adjusted odds ratios, *CI* confidence intervals, *HDRS* Hamilton Depression Rating Scale, *SE* standard error

*$p<0.05$; **$p<0.01$; ***$p<0.001$

older participants (a$\beta=0.32$; 95% CI − 0.24; 0.88; $p>0.05$). Similarly, a one-unit decrease in HDRS score was associated with a 0.67-unit decrease in suicide score among the 'antenatal only' trajectory group (95% CI 0.23; 1.11; $p<0.01$), but this association was only marginal among the 'antenatal and postnatal' trajectory groups (a$\beta=0.95$; 95% CI − 0.09; 1.99; $p>0.05$).

Discussion

Our study sought to investigate the longitudinal association between depressive symptoms and suicidal risk among perinatal women at risk for depression during pregnancy and living in a low-income informal settlement near Cape Town. Overall, our results indicate that change in depressive symptom severity was associated with change in severity of suicidal risk. However, this association was only present when depressive symptom scores decrease. In other words, a decrease of 11 points on the HDRS score, thought to be associated with patients' self-report of having much improved [44], was associated with an 8-point decrease in suicide scores (i.e., a clinical improvement in suicidal risk severity), but a worsening of depressive symptoms was not associated with change in suicidal risk severity. One may argue that this may reflect the protective perinatal stage that has been mentioned in previous research [5, 45], especially given that this pattern of association did not differ

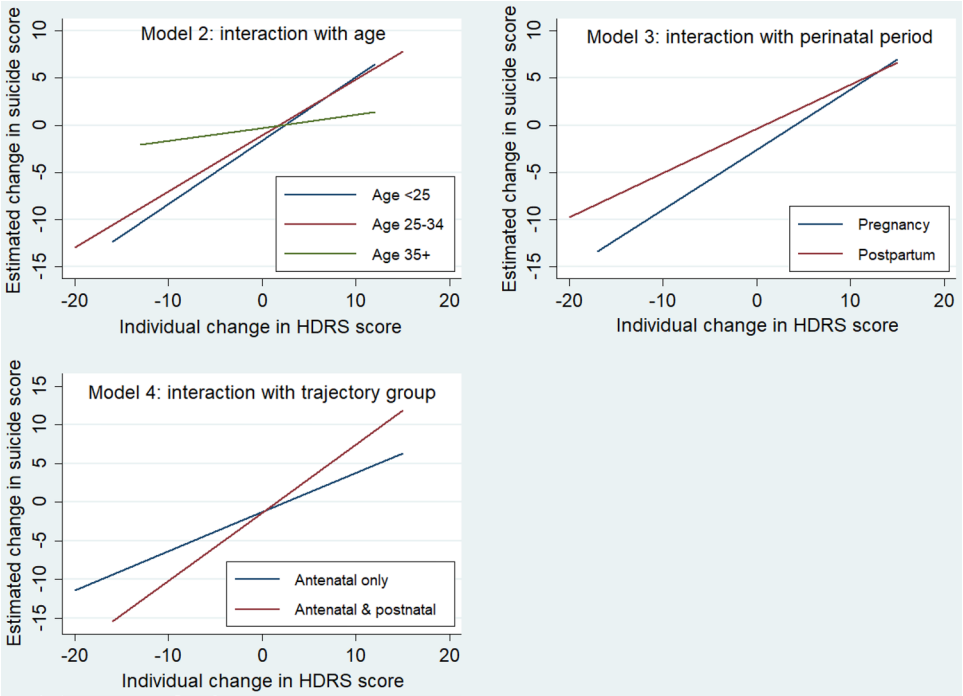

Fig 1 Interaction of change in HDRS scores with age, perinatal stage, and trajectory group in predicting change in suicide scores

from pregnancy to the postnatal period. A longer follow-up would have enabled us to assess whether this association differed after 12-month postpartum, compared to during the perinatal stage.

The longitudinal association between depressive symptoms and severity of suicidal risk was moderated by age and trajectory type: while a decrease in depressive symptoms was associated with a decrease in severity of suicidal risk among women aged 18–34 years, and among those whose depressive symptoms decreased over the course of the perinatal period, this was not the case among older women and those with more severe depressive symptoms throughout the perinatal period. One explanation for this finding could be that for some women, suicidal risk took longer to abate following a decrease in depressive symptoms; a possibility which we could not assess, since we analyzed simultaneous change in depressive symptoms and severity of suicidal risk, from one assessment to the next. Indeed, our previous work indicated that women from the 'antenatal and postnatal' trajectory group were at higher risk of suicide at baseline [25]. Yet, a study in the US among adults suffering from depression and on antidepressants showed that it took longer for suicidal behaviors to subside, following a decrease in depressive symptoms, among those who initially reported greater risk of suicide [46].

Alternatively, our findings could indicate that depression and suicidal risk are not necessarily associated for all perinatal women. For instance, women belonging to the 'antenatal and postnatal' trajectory group reported poorer social and economic circumstances and poorer clinical features during pregnancy [25]. Given the common risk factors for suicide and depression, the results could indicate that these risk factors had a direct impact on women's course of suicidal risk, independent of depressive symptoms. Suicidal risk among the 'antenatal only' trajectory group, on the other hand, may not necessarily be an indicator of future suicidal behavior, but reflect transient endorsements of suicidal thoughts as an expression of general initial distress associated with pregnancy (e.g., HIV-positive status, and lack of support from partner or family), which subsides alongside depressive symptoms as women and their families accept the pregnancy. In the present study, the incidence of suicidal ideation, plan, or attempt was too small to meaningfully assess the association between such behaviors and depressive symptoms over time. It is, therefore, not possible to say whether the pattern of association found in our study relate to suicide risk in general, or whether it is specific to suicidal thoughts or actual suicidal behavior, such as self-harm or suicide attempts. However, there is evidence from a nationally representative South African survey, suggesting that only 31.7% and 11.2% of individuals reporting suicidal ideation eventually make a suicide attempt, with and without a plan, respectively, and that anxiety and impulse-related disorders were stronger risk factors for suicide attempts among people with suicide ideation than major depression [47].

In fact, there is emerging evidence, mostly from high-income countries, that there are heterogeneous profiles of symptoms among people diagnosed with depression, which differ in terms of severity and endorsement of anxiety and self-harm symptoms [48]. While this was beyond the scope

of this study, it could be that the lack of association between depressive symptoms and suicidal risk among older women or those who report more severe and chronic depressive symptoms, such as in the 'antenatal and postnatal' trajectory group, reflects a type of depressive symptomatology which is independent of suicidal ideation.

Altogether, our findings indicate that depressive symptoms and risk of suicide were only associated when depressive symptoms decreased, and that among younger women and among those who showed milder depressive symptoms over the course of the perinatal period. This supports the idea that, among women at risk for depression during pregnancy, depression and suicidal risk are overlapping but separate entities. This has direct implications on the treatment and monitoring of perinatal women at risk for depression over time—in both research and clinical contexts. Indeed, this means that women may still be at risk for suicide even if depressive symptoms decrease. It is, therefore, essential to assess both phenomena independently, as suggested by Nock et al. [22] in their global review of the literature on mental disorders and suicidal behaviors.

In our study, of the 23% of the pregnant women recruited who were at risk for suicide, over a quarter did not have a diagnosis of depression. This contrasts with Dewing et al. [15] study, where 8% of pregnant women from Khayelitsha reported mild-to-severe risk of suicide on the MINI suicidality module, and with Onah et al. [7] study, where 18% of pregnant women living in a nearby informal settlement reported suicidal ideation or behavior, at least half of which did not suffer from depression, anxiety or personality disorder. The different profile of suicidal risk reported in our study is likely due to the high-risk nature of the sample, since all women screened positive on the EPDS and, thus, at risk for depression. We acknowledge that women were screened with the EPDS which included a suicide/self-harm item, so the sample may be biased. However, when the self-harm item was excluded from the total EPDS score at recruitment, only 5% of women scored below the cut-off of 13 (between 10 and 12). Therefore, our sample is likely to still be a high-risk group for depression, regardless of suicidal risk. Given the above evidence, we could assume, then, that the identification of depression and suicidal risk should also be done separately, even all women, irrespective of their depressive symptom severity during pregnancy.

Some have argued that assessing suicidal risk is less reliable when done in the context of a screening tool for depression, compared to when it is assessed independently [5]. However, the risk of suicide in research studies is often measured using a single item which is included in most screening tools used for perinatal depressive symptoms [15, 18], which is not ideal given our findings. There is some evidence from the United Kingdom that endorsing 'Yes, quite often' to the self-harm item on the EPDS is strongly associated with a diagnostic assessment of suicidal risk [49]. In South Africa, Rochat et al. [6] also reported that the self-harm item on the EPDS had good sensitivity and specificity among women living in a rural area in Kwa-Zulu Natal. This, however, was not the case in the present study, where neither the EPDS nor the HDRS suicide items were well correlated with suicidal ideation or suicidal risk assessed with the MINI (results not presented here).

There are no formal identification or monitoring mechanisms for depression or suicidal risk in clinical settings in South Africa [50], other than when conducted through NGOs or donor agencies [51], most of which use depression screening tools similar to the EPDS. However, three screening questions are to be included in the next version of the maternity case records, which are forms that are completed by nurses for all pregnant women at each antenatal visit. Two of these questions relate to mood and one to suicidal behaviors, and will be asked by nurses only in circumstances where a referral system and mental health services are available. Women who endorse the suicide item, suggesting the presence of suicidal ideation and plan, will be referred immediately, regardless of their responses on the other two mood-related questions. Therefore, this tool could be used as a way to identify and monitor women at risk for depression or suicide, though the sensitivity of a single item in identifying women at risk of suicide remains to be assessed.

Our study has several limitations which should be acknowledged. First, depressive symptoms were self-reported, which is known to be less reliable than formal assessments [2]. In addition, while the suicidality module of the MINI has been used in the previous studies assessing suicidal risk among populations in Khayelitsha, its validity remains to be assessed in this context. Results from a qualitative study conducted in Khayelitsha indicated that symptoms of depression described by depressed and non-depressed pregnant women were consisted with those included in the DSM-V and ICD-10 classifications [52]. Thus, there is little reason to believe that the suicidality module would not also be clinically meaningful in this population. However, cultural context remains important in the etiology of suicidal behaviors [13, 53], so our findings are unlikely to be generalizable to other LMICs, or other populations within South Africa. Second, the aim of our paper was not to identify risk factors involved in the complex pathways to suicidal behaviors, so we did not control for any demographic variables, other than age, as suggested in the previous reviews of the literature [13, 54]. However, we ran post hoc analyses to ensure that the modifying effect of age was not confounded by number of children in the mothers' care—a factor which could become decisive for women reporting suicidal ideation. Third, GEE is a method of analyses that generates population-average estimates. Given the complex etiology of depressive symptoms and suicidal behaviors, other

methods of analysis, such as multilevel modelling, could provide some valuable insights into individual differences in the longitudinal association between depressive symptoms and severity of suicidal risk. Finally, despite the lack of differences in the severity of suicidal risk and depressive symptoms between the control and treatment groups over time, the intervention may have had an impact on our results. To assess this possibility, the same analyses were conducted separately for control and intervention participants. Results were very similar, though the interaction identified between change in depression scores and age was no longer present among intervention participants alone. Further research is, therefore, needed among a more general cohort of perinatal women to support our findings.

Conclusion

Our study sheds light on the association between depressive symptoms and suicidal risk over the perinatal stage, and highlights the importance of considering depression and suicide as overlapping but relatively independent phenomena. Our study also contributes towards identifying high-risk groups for preventive strategies among low-income perinatal women at risk of depression or suicide. Given that suicidal ideation remains a predictor of suicide attempts within a year of ideation onset among South Africans [47], it is essential that pregnant and postnatal women at risk of suicide are identified and monitored independently from risk of depression, so that suicidal behaviors are prevented, and the related health and economic burden avoided. Including screening for suicidal risk as part of antenatal care is one step in the right direction, but further efforts should go into understanding the pathways towards suicidal behaviors and depressive symptoms among high-risk perinatal groups in LMICs.

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Compliance with ethical standards

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

Ethical standards All participants recruited in the randomized-controlled trial and included in the present study provided informed written consent. The original randomized-controlled trial received ethical approval from the University of Cape Town (UCT)'s Human Research Ethics Committee (HREC REF 226/2011), and so did this present study (HREC REF 835/2015).

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