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Factors associated with pregnancy-related anxiety in Tanzanian Women: a cross sectional study

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Title: Factors Associated with Pregnancy-Related Anxiety in Tanzanian Women: a cross sectional study

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ABSTRACT

Objective: To identify factors predictive of pregnancy-related anxiety (PRA) among women in Mwanza, Tanzania.

Design: A cross sectional study was used to explore the relationship between psychosocial health and preterm birth.

Setting: Antenatal clinics in the Ilemela and Nyamagana districts of Mwanza, Tanzania.

Participants: Pregnant women less than or equal to 32 weeks' gestational age (N=212) attending the two antenatal clinics.

Measures: PRA was measured using a revised version of the 10-item PRA Questionnaire (PRA-Q). Predictive factors included social support (Multidimensional Scale of Perceived Social Support), stress (Perceived Stress Scale), depression (Edinburg Postpartum Depression Scale), and socio-demographic data. Bivariate analysis permitted variable selection while multiple linear regression analysis enabled identification of predictive factors of PRA.

Results: Twenty-five percent of women in our sample scored 13 or higher (out of a possible 30) on the PRA-Q. Perceived stress, active depression, and number of people living in the home were the only statistically significant predictors of PRA in our sample.

Conclusions: Our findings were contrary to most current literature which notes socio-economic status and social support as significant factors in PRA. A greater understanding of the experience of PRA within the social cultural context of low- and middle-income countries and its predictive factors is needed in low- and middle-income countries to support the development of PRA prevention strategies.

ARTICLE SUMMARY

Strengths and limitations of this study

- This is the first study to examine predictive factors for PRA among pregnant women in Tanzania.
- This study identifies the importance of cultural context when examining PRA among pregnant women in LMIC.
- There are no standardized screening tools for PRA or commonly accepted categorization methods for the tools available making it difficult to compare findings between studies or compare characteristics between levels of severity of PRA. However, findings of this study were stable across continuous and categorical PRA measurements.
- Convenience sampling was employed and consequently results cannot be generalized to all pregnant women in the Ilemela and Nyamagana districts of Tanzania.
- The lack of comparable studies in LMIC makes it difficult to identify potential anomalies in these findings.

INTRODUCTION

Pregnancy-related anxiety (PRA) is characterized by anxiety pertaining to the pregnancy, including labour and delivery, the fetus or infant's health, the mother's health, accessibility and quality of health care resources, and/or the ability to parent.[1-4] PRA is a distinct and different phenomenon than general anxiety occurring concurrent to pregnancy [1] and has stronger correlations to preterm birth (PTB) (birth at less than 37 weeks' gestation) than more commonly studied general anxiety or depression.[2, 4-6] An estimated 85% of PTB globally, occur in Africa and Asia.[7] Africa has the highest rate of PTB where some regions reach 17.5%;[7] approximately 14.3% of births are preterm in Eastern Africa.

PRA prevalence estimates in high-income countries range from 6 - 29%;[8-11] however, high-risk populations tend to yield higher rates of PRA.[9] Among a sample of pregnant women from Tanzania (a low-income country [12]), in the city of Mwanza, the rate of PRA was 18.3%, which was associated with antenatal depression (odds ratio 1.36, 95% confidence interval 1.23 to 1.5).[13, 14] In the lower-middle income country of India,[12] in the city of Kerala, prevalence of severe PRA ranged from 0.4% to 22% depending on the trimester, but at least 74% of Indian women experienced moderate levels of PRA in all trimesters.[15]

Within high-income countries, non-Caucasian ethnicity, low family income, and limited social supports are consistently noted as prominent risk factors for PRA.[2, 16, 17] In low-and-middle-income countries (LMIC), it is unknown if these remain the most prominent risk factors for PRA. In Tanzania, 67% of the population falls below the poverty line and 99% of Tanzanians are of African ethnicity.[18] Moreover, 69% of the population lives in rural areas and there are only

three physicians per 100000 people [18] which may result in concerns related to healthcare resources which further contributes to the potential for PRA. As such, it seems reasonable to anticipate PRA prevalence in low- and middle-income countries such as Tanzania may be comparable to PRA rates in high-risk populations within high-income countries.

Unfortunately, there is a dearth of literature examining PRA in LMIC; only 8% of LMIC are represented in literature regarding all common mental illness during the prenatal period.[19] This lack of contextually relevant literature makes it difficult to develop practice guidelines or protocols to address PRA in these countries. Moreover, in many LMIC like Tanzania, many women come from similar socioeconomic backgrounds and it remains unclear why some women develop severe PRA and others do not. Alternative theories of stress can offer insight about stressful events, such as PRA, in unexamined populations. Lazarus and Folkman [20] suggest that stress occurs when people are faced with a situation they deem a possible threat and cannot access the resources required to manage the threat. In accordance with this theory, the differences in sociocultural context between high-income countries and LMIC may be that LMIC hold different risk factors for PRA than high-income countries. Differences in countries' public health education may alter the amount of anxiety women have about the physical symptoms of pregnancy as they are more or less aware of what to expect and what is normal.[21] Moreover, difference in accessibility to health care services can affect women's appraisal of whether or not adequate prenatal care is attainable. This doubt can increase concerns about pregnancy complications, delivery, or infant care, particularly if access to healthcare is limited or women have had previous negative healthcare experiences.[2] Consequently, factors associated with PRA in high-income countries should not be assumed true for LMIC.

We used the Social Ecology Model for Health Promotion [22] to identify predictive factors. The Model proposes health promotion is most effective when we consider the interaction of peoples' attributes and both their physical environment and social climate.[22] As people change their environment it will contribute to their change in health. In this model, the notion of "environment" is multidimensional and can include tangible attributes (i.e. upsetting events in the community) or social constructs, objective qualities or perceived qualities, and/or social climate or physical surroundings.[22] Additionally, the Social Ecology Model for Health Promotion asserts that human-environment interactions should be considered on both small and large scales (e.g. individuals, families, communities, and populations).[22] Therefore, in order to thoroughly examine factors associated with PRA in women in the low-income country of Tanzania, we examine attributes of pregnant women, their families, their communities and their environment. We sought to answer the research question: what predictive factors are associated with PRA for women attending antenatal clinics in the Ilemela and Nyamagana districts of Tanzania, Africa.

METHODS

Study design

We used data collected during women's first attendance at prenatal clinic (gestational age 6-32 weeks). These women were enrolled in a prospective longitudinal study that explored the relationship between psychosocial health and preterm birth among women in Mwanza, Tanzania.[23] A collaborative research team comprised of faculty and graduate students, from University of Calgary and Catholic University of Health and Allied Sciences (CUHAS) in

Mwanza, Tanzania and local registered nurses who also served as field workers, collected data at four time points throughout participants' pregnancies (first trimester, early second trimester, late second trimester, and early third trimester). During the first time point, women were coached to return to the clinic every six weeks until 32 weeks gestation, then were seen at delivery and again 6 weeks postpartum.[23] At each point of contact participants received a perinatal mental health assessment; private space was provided to complete questionnaires.[23] The Conjoint Health Research Ethics Board at the University of Calgary (approval numbers REB 13-0399 and 16-1579), and the Catholic University of Health and Allied Sciences/Bugando Medical Centre Research Ethical Committee (CREC/062/2013) approved these studies (i.e., primary and secondary analysis). The larger study was also approved by the Tanzania National Institute of Medical Research - Lake Zone Institutional Review Board (MR/53/100/254 and MR/53/100/160).

Setting and participants

A convenience sample of 212 women was recruited, using a systematic sampling approach, from antenatal clinics in the Ilemela (n=72) and Nyamagana (n=140) districts of Tanzania from June 2013-January 2015.[23] The sample was comprised of women who spoke Swahili or English, and were 32 weeks' gestational age or less at the time of enrollment based on women's last menstrual period. Adolescent mothers were included as they were classified as emancipated minors.[23] Women who self-reported co-morbidities such as hypertension, diabetes, malaria or human-immunodeficiency virus (HIV) were not excluded due to the prevalence of these illnesses. Recent work within this sample revealed that the high prevalence of HIV coupled with minimal health knowledge has resulted in women with and without HIV sharing similar concerns

about the illness and potential effects on their baby.[21] The nurse in-charge was the first to approach and invite participation from eligible women in the waiting room of the antenatal clinics. A member of the research team then obtained informed consent from women who agreed to participate (see image file for Figure 1 Recruitment flow diagram).[23]

Data collection

A general questionnaire was used to collect socio-demographic data including age, education, income, and co-morbidities.[23] PRA was measured using a revised version of the 10-item PRA Questionnaire (PRA-Q) that assesses feelings about health during pregnancy, infant or baby's health, and labour and delivery.[24, 25] Each item was a 4-point Likert scale of 0-3; a cumulative score was given out of a possible 30 points.[24] Information on household incomes was difficult to obtain due to cultural norms and traditions.[13] Consequently, socio-economic welfare was assessed using a Likert scale questionnaire focused on the acquisition of assets (e.g. car, motorcycle, bicycle), living standards (e.g., access to water, and number of meals eaten per day), and other wealth status (e.g., employment).[13, 26] Most questions were dichotomous (yes or no) with an associated score of one or two with the exception of three questions; roof type and meals per day provided three possible answers with associated scores of one to three and water source had five possible answers with scores from one to five. The final score on the Socio-Economic Welfare Questionnaire (SEW-Q) was a sum of all the answers for a maximum possible score of 29. Social support was rated using the 12-item Multidimensional Scale of Perceived Social Support.[27] This scale includes questions about the relationship of supportive people to the participant, the perceived level of support the participant receives from her support network, and the extent to which the participant feels cared for by the people closest to her.[27]

This scale has high internal consistency reliability (Cronbach's $\alpha > 0.90$). Perceived stress (PS) was measured with a 10-item tool (4-point Likert scale) examining the frequency of increased stress, perceived level of control over their life and stressful events, and ability to cope with stress. A cumulate score was given out of a possible 40 with higher scores indicating increased stress.[28] Evaluation of the PS scale has consistently shown adequate reliability (Cronbach's $\alpha > 0.70$) and has been used with a variety of populations and translated into 25 languages.[29] However, empirical evaluation has not been completed on these translated versions or with populations other than college students or the employed.[29] The Edinburgh Postnatal Depression Scale (EPDS), a self-reported 10-item scale was used to screen for depression and identify at-risk mothers. Empirical evaluation demonstrates good reliability (Cronbach's $\alpha=0.83$) [30]. This scale has been extensively tested in both pregnant and postnatal populations and is widely accepted for global populations with translations in several languages.[31, 32] It should be acknowledged that none of the tools used in this study have been tested on the population of interest.

Statistical analysis

For bivariate analysis, variables of interests (Table 1) were selected based on factors identified in the current literature, the theory of cognitive appraisal,[20] and the social ecological model for health promotion.[22] Bivariate analyses identified which continuous variables had a relationship with the PRA total score. Nominal variables with more than two values (i.e. marital status, occupation) were converted into dichotomous variables (i.e. in relationship or not) and analyzed with Mann-Whitney U tests as PRA was not normally distributed. Converted variables found to have a significant association with PRA total score were then expanded and each variable's

Table 1. Variable selected for bivariate analysis

Individual	Family	Community
EPDS Score *	Sum of SEW-Q Score *	Events in the Community Upsetting to You
Age of participant	Gravidity	Perceived Social Support Score
Mother Born in Mwanza	Current Marital Status **	Healthcare Facility
Mother's highest level education	Mother's Main Occupation	
PS Score *	Father's Main Occupation	
History of Hypertension	Father's Highest Level of Education *	
History of Depression *	Total Number of Pregnancies	
History of Gestational Diabetes	Total Number of Live Births	
History of Schistosomiasis	Previously Had Preterm *	
History of Syphilis	Previously Had a Male Baby	
History of HIV *	Number of People Living in the Home *	
History of Malaria	Planned Pregnancy *	
History of Anemia	Gestational Age at First Visit	

*Predictor variable in regression analysis
**Married and Separated were dichotomized predictor variables in regression analysis

original values (i.e. coupled, married, common-law, divorced, etc.) were analyzed as separate dichotomous variables using Mann-Whitney U test for an association with PRA total score. Ordinal variables (i.e. education) were analyzed with Kruzkal-Wallis tests as PRA was not normally distributed. Variables with a significance level of $p \leq 0.25$ in the bivariate analyses were included in the multiple linear regression analyses.[33] Variables known to have clinical relevance such as socio-economic welfare score and marital status were also included regardless of their statistical significance.

Multiple linear regression modeling was employed with PRA total score as the dependent variable. In order to assess variables associated with the most severe cases of PRA, PRA scores were divided into quartiles and only cases with PRA scores in the top and bottom quartiles were analyzed in this multiple regression analyses. Given the rigorous variable selection process, a backwards input method was used. Variables were then removed starting with the variables that were least statistical significant. A two-sided p value of ≤ 0.05 was considered statistically significant for all multiple linear regression analyses. Residual of error values were then examined in a scatter plot, Q-Q plot, and histogram to verify the assumptions of normal distribution and homoscedasticity were satisfied.

We conducted supplemental analyses to provide a comparison with the primary analyses which only used cases with PRA scores in the first and fourth quartile. The first supplemental analysis employed the same multiple linear regression process as the primary analysis but included all PRA scores. We employed the same variable selection method described in the primary analysis. Currently there is no empirically tested, or commonly accepted, method for operationalizing PRA-Q scores into levels of severity. Thus, our primary analysis maintained rigor by leaving these scores as a continuous variable. To evaluate how our results may compare to studies that have categorized PRA scores, we completed a second supplemental analysis. Using all 212 cases, PRA scores were dichotomized in accordance with the work of Fairlie et al.;[34] high-anxiety was defined as three or more answers of "3" (very much) on the PRA-Q. All other scores were categorized as low-moderate anxiety. Bivariate and χ^2 tests were conducted where appropriate, to identify factors associated with high, or low-moderate PRA.

RESULTS

The sample was comprised of 72 women from the Ilemela district and 140 women from the health center in Nyamagana (*N*=212) with a median age of 26 years (range 16 – 44 years). Approximately three-quarters of participants (78.2%) were multiparous, the majority of participants were in a relationship (89.6%), and over three-quarters of participants (77.8%) identified that they were married. Although nearly all participants (97.2%) had some level of formal education, most had only completed primary school (64.6%). Socio-economic status was higher than expected with 57.1% of participants scoring 12 or better (out of 18) on the SEW-Q and 9.0% scoring five or less. PRA-Q scores ranged from 0-24 with a median score of 10 (inter quartile range (IQR)=8-13). When PRA was dichotomized as "high" and "low-moderate" categories, 6.1% of participants (n=13) had high anxiety. Table 2 shows the demographic characteristics and PRA scores of the study's sample.

Table 2. Demographic characteristics

	Total N=212	Nyamaganan n=140 (66%)	Ilemelan n=72 (34%)
	Median (range)	Median (range)	Median (range)
Age (years)	26 (16-44)	33 (16-44)	29 (17-40)
GA (weeks) at 1st visit	24 (6-32)	23 (6-32)	26 (8-32)
	N (%)	n (%)	n (%)
Primiparous	50 (21.8)	33 (21.6)	17 (22.7)
Born in Mwanza	71 (33.5)	52 (37.1)	19 (26.4)
Primary Education	137 (64.2)	104 (74.3)	33 (45.8)
> Primary Education	69 (32.5)	33 (23.6)	36 (50.0)
Married	165 (77.8)	105 (75.0)	60 (85.7)
Employed	138 (60.3)	92 (60.1)	46 (61.3)
	Median (range)	Median (range)	Median (range)
Sum of SEWQ Scores	12 (2-18)	12 (2-18)	13 (2-16)
Perceived Social Support Score	59 (20-84)	59 (21-84)	59 (20-80)
Perceived Stress Score	19 (1-36)	18 (1-36)	21 (8-33)
PRA-Q total Score	10 (0-24)	10 (0-24)	12 (2-24)

GA=gestational age; SEWQ=Socio Economic Welfare Questionnaire; PRA-Q=pregnancy-related anxiety questionnaire

In the primary analysis, PRA scores were quartiled and only cases from the first and fourth quartile were used (n=90). The first quartile scores ranged from 0-7 and the fourth quartile scores ranged from 13-24. The variables included in the multiple linear regression analyses are shown in Table 1. The results of the primary regression (Table 3) indicated that PS score, EPDS score, and number of people living in the home were significant predictors of PRA (R^2=0.339, F(3,74)=12.657, p=0.000) (adjusted R^2=0.312). PS score and EPDS score were positively associated with PRA score, whereas the number of people living in the home was negatively associated with PRA score. There was no indication of multicollinearity as each of these predictors met the criteria for statistical significance ($p \leq 0.05$), had a Variance Inflation Factor of less than 2, and a Tolerance greater than 0.05. While the EPDS is supposed to measure postpartum depression, there is concern the scale contains an anxiety subscale.[35] To account for a potential spurious relationship between this anxiety subscale and PRA, the EPDS scores were recalculated, excluding the scores for two anxiety-related questions. Bivariate analysis indicated the recalculated EPDS scores and full EPDS scored shared the same correlation with PRA score (r_s=0.511, p=0.000). When the linear regression modeling was re-run using the recalculated EPDS scores the model summary was only marginally changed (R^2=0.338, F(3,74)=2.607, p=0.000) (adjusted R^2=0.311). The total of the two anxiety questions from the EPDS was analyzed as a separate variable. This variable showed a positive correlation with PRA scores (r_s=0.422, p=0.000) but was not a statistically significant predictor in the regression models.

Table 3. Regression model of factors associated with PRA score

	B	*SE B*	β	*t*	*p*
PS Score	0.306	0.121	0.328	2.527	0.014
EPDS Score	0.328	0.136	0.316	2.416	0.018
Number of people living in home	-0.718	0.342	-0.204	-2.102	0.039

In the first supplemental analysis (using all cases, n=212), PRA had a significant association ($p \leq 01.05$) with EPDS score, recalculated EPDS score, PS, SEW-Q score, a history of HIV, and healthcare facility. The results of this regression analysis were similar to the regression modeling using the first and fourth quartile PRA scores; results indicated PS score and EPDS score were statistically significant predictors of PRA (R^2=0.196, F (2,209)=25.394, p=0.000) (adjusted R^2=0.188). Both PS score and EPDS score maintained a positive correlation with PRA. This regression was re-run using the recalculated EPDS scores and the model summary was again only marginally different (R^2=0.195, F(2,209)=25.243, p=0.000) (adjusted R^2=0.187) with the same final predictors.

In the second supplemental bivariate analysis with dichotomized PRA, the number of people living in the home, PS score, and EPDS scores showed significant associations ($p \leq 0.05$) with high or low-moderate PRA. Fisher's Exact test showed PRA to have a significant association with if the mom was born in Mwanza, and if the pregnancy was planned. Eighty-five percent (n=11) of the participants with high anxiety had not planned their pregnancy. X^2 analysis showed presence of depression (an EPDS score of 13 or higher [31]) was two-fold in women with a high PRA scores (53.8%) compared to women with low PRA scores (27.1%) (p=0.04). When EPDS scores were recalculated without the anxiety questions, the presence of depression remained about two-fold in women with high PRA scores compared to women with low PRA scores

(23.1% and 11.6% respectively). However, these results were not statistically significant (p=0.203).

DISCUSSION

Twenty-five percent of women in our sample scored 13 or higher (out of a possible 30) on the PRA-Q, and 6.1% of participants met the threshold for "high anxiety".[34] Regardless of how PRA was operationalized (continuous, dichotomized, or limited to only the highest and lowest scores), EPDS score and PS score consistently had a positive correlation with PRA and were significant predictors in the regression models. Current literature substantiates the identified association between depression and PRA.[1, 13] Pregnant women more commonly experience co-morbid anxiety and depression rather than one of these afflictions alone.[13, 36] However, there appears to be limited understanding of why this comorbidity exists and which develops first, depression or anxiety. Consideration of the Theory of Stress, Appraisal, and Coping [20] combined with the nuances of this sample's cultural context provides insight in this inquiry. Lazarus and Folkman [20] posit that stress results when an event is appraised as a possible threat to one's well-being and the resources to mitigate the event are deemed unattainable. Moreover, factors such as novelty and time proximity to the event can affect the perception of the threat's severity.[20] In accordance with this theory, the lack of basic health knowledge, coupled with restricted access to healthcare facilities, and the low socio-economic standing of most Tanzanians creates an environment where pregnancy could commonly result in stress or anxiety.[18, 21] Moreover, social customs in Tanzania deter the discussion of personal matters with anyone: friends, family, or spouses.[21] A phenomenological study used a subsample of our participants to explore moderate to severe PRA. This study identified common feelings of

isolation and alienation amongst participants as their anxiety worsened and there was no perceived acceptable forum to discuss their fears; ultimately, women endorsed the isolation evolving into sadness.[21, 37] Even in cases where women surrounded themselves with family, there was still a reluctance to discuss their concerns. Our primary analysis revealed a negative correlation between number of people living in the home and PRA. More people in the home increases the likelihood that the mother has someone she may feel comfortable talking to. It is therefore conceivable that in this populace, severe PRA may trigger an internal conflict of wanting to express these fears while worrying that this is not acceptable, which results in feelings of isolation and subsequent depression.

Interestingly, the factors most commonly associated with PRA in current literature did not hold significance in this study. Socio-economic welfare score showed a significant correlation with PRA only when all participants were used and PRA was a continuous variable. When PRA scores were dichotomized or only participants with the PRA scores in the first and fourth quartile were used, the correlation with socio-economic welfare score lost statistical significance, and did not show significant predictive properties. Perceived social support score, marital status, and mother's occupation also failed to have a significant association. Active depression is the only factor found to predict PRA in our study which is also consistently correlated to PRA in current literature.[1, 13] Our findings are remarkably contrary to the current literature, which consistently lists social supports, ethnicity, and economic status as key risk factors.[2, 16, 17] These gross variations from current research may reflect the limited research available from LMIC.[19] Moreover, our findings serve as a caution to generalize findings on PRA from high-income countries to populations in LMIC.

Despite the vast differences in culture and socioeconomic standing it makes sense that globally, women can experience the same condition, PRA, for different reasons. The notion of novelty can critically change the perceived threat in an event.[20] Pregnancy may be uniquely novel in its accompaniment of physiological and psychological emotional investment coupled with the distinct outcome of creating human life. One possible explanation is that pregnancy may hold an unparalleled element of novelty (thus propensity to induce anxiety) regardless of a women's background or gravidity. Differences in social norms and fundamental values, however, may change what someone considers threatening or stressful.[20] In the context of this study, socio-cultural norms such as dynamics between men and women may change the effect of social supports on PRA scores. The subsample of women enrolled in the phenomenological study of PRA often described their husbands growing distant during the pregnancy, which had an exacerbating effect on their anxiety rather than calming [21]. Many of the fears voiced by women in Tanzania were due to limited basic health and pregnancy knowledge; many times normal sensations resulted in fear of death for the mother or baby.[21] These differences in findings outline the need for more research exploring the notion of PRA in LMIC and between LMIC and high-income countries.

Limitations

Convenience sampling was employed and consequently results cannot be generalized to all pregnant women in the Ilemela and Nyamagana districts of Tanzania. Moreover, the lack of comparable studies in LMIC makes it difficult to identify potential anomalies in these findings. There are no standardized screening tools for PRA or commonly accepted categorization

methods for the tools available [38] making it difficult to compare findings between studies or compare characteristics between levels of severity of PRA. Moreover, within current literature there is no empirically tested way to operationalize PRA scores. The PRA-Q examines broad concepts of PRA making it an effective screening tool but difficult to identify severity of PRA or clinical diagnoses.[38, 39] This was a secondary data analysis limiting variable options to those already included in the longitudinal study. Findings in the regression modeling only explain 20-34% of the change in PRA scores across our sample. Consequently, there are still significant factors not identified in this study.

CONCLUSION

Active depression is one of the only factors consistently correlated to PRA in both our study and current literature. Given the socio-cultural differences between populations in high-income countries and LMIC, the unique psychological complexities of pregnancy, and the personal nature of how people assess events as stressful, findings should not be generalized across these populations. Ultimately, more research is needed on PRA universally and the reason for comorbidity between depression and PRA. In LMIC, before predictive factors and prevention strategies can be identified, further fundamental exploration of PRA is needed to better understand how this phenomenon fits within these socio-cultural settings.

Contributions: VW, and SSP worked together to develop the research question, study design, and analytic plan. SSP, NL and GM provided consultation from the research design through to the manuscript development, and directed the analysis of the study. ECN, local lead in Mwanza,

translated documents, obtained ethics approval, and supervised research assistants. All authors have contributed to the work and approved the manuscript.

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Data sharing statement: The dataset generated during our study are not publicly available as consent for secondary use was not obtained from study participants. Please contact the corresponding author for additional information.

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LEGEND

Tables

- Table 1. Variable selected for bivariate analysis
- Table 2. Demographic characteristics
- Table 3. Regression model of factors associated with PRA score

Figures

- Figure 1. Recruitment flow diagram

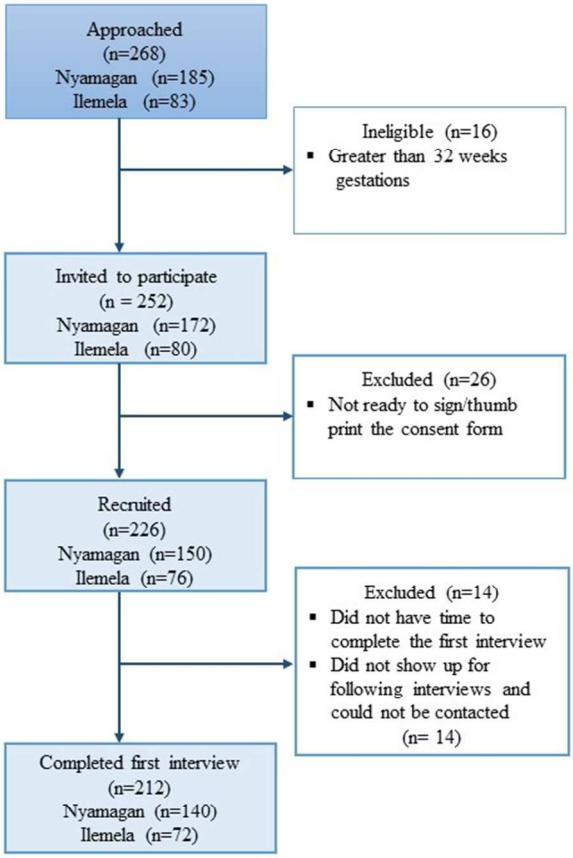

Figure 1. Recruitment flow diagram

190x254mm (96 x 96 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7-8
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-9
Bias	9	Describe any efforts to address potential sources of bias ***(systematic sampling to reduce selection bias)***	7
Study size	10	Explain how the study size was arrived at ***(convenience sample)***	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-11
		(*b*) Describe any methods used to examine subgroups and interactions	11
		(*c*) Explain how missing data were addressed	N/A
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	N/A

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses ***(supplemental analyses conducted)***	11
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	12
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	12-13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-14
		(*b*) Report category boundaries when continuous variables were categorized	12-13
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Factors associated with pregnancy-related anxiety in Tanzanian Women: a cross sectional study

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ABSTRACT

Objective: To identify factors predictive of pregnancy-related anxiety (PRA) among women in Mwanza, Tanzania.

Design: A cross sectional study was used to explore the relationship between psychosocial health and preterm birth.

Setting: Antenatal clinics in the Ilemela and Nyamagana districts of Mwanza, Tanzania.

Participants: Pregnant women less than or equal to 32 weeks' gestational age (N=212) attending the two antenatal clinics.

Measures: PRA was measured using a revised version of the 10-item PRA Questionnaire (PRA-Q). Predictive factors included social support (Multidimensional Scale of Perceived Social Support), stress (Perceived Stress Scale), depression (Edinburg Postpartum Depression Scale), and socio-demographic data. Bivariate analysis permitted variable selection while multiple linear regression analysis enabled identification of predictive factors of PRA.

Results: Twenty-five percent of women in our sample scored 13 or higher (out of a possible 30) on the PRA-Q. Perceived stress, active depression, and number of people living in the home were the only statistically significant predictors of PRA in our sample.

Conclusions: Our findings were contrary to most current literature which notes socio-economic status and social support as significant factors in PRA. A greater understanding of the experience of PRA within the social cultural context of low- and middle-income countries and its predictive factors is needed in low- and middle-income countries to support the development of PRA prevention strategies.

ARTICLE SUMMARY

Strengths and limitations of this study

- This is the first study to examine predictive factors for PRA among pregnant women in Tanzania and identifies the importance of cultural context when examining PRA among pregnant women in LMIC.
- This study used secondary data limiting variable options to those already included in the primary longitudinal study.
- There is no established normative reference to indicate when a woman is at "high risk" for PRA. Thus factors identified in this study should only be considered in relation to relative (i.e., higher or lower) PRA scores.
- Convenience sampling was employed and consequently results cannot be generalized to all pregnant women in the Ilemela and Nyamagana districts of Tanzania.
- The sample size of the current study may have limited the power of some of the statistical analysis making it difficult to make inferences.

INTRODUCTION

Pregnancy-related anxiety (PRA) is characterized by anxiety pertaining to the pregnancy, including labour and delivery, the fetus or infant's health, the mother's health, accessibility and quality of health care resources, and/or the ability to parent.[1-4] PRA is a distinct and different phenomenon than general anxiety occurring concurrent to pregnancy [1] and has stronger correlations to preterm birth (PTB) (birth at less than 37 weeks' gestation) than more commonly studied general anxiety or depression.[2, 4-6] An estimated 85% of PTB globally, occur in Africa and Asia.[7] Africa has the highest rate of PTB where some regions reach 17.5%;[7] approximately 14.3% of births are preterm in Eastern Africa.

PRA prevalence estimates in high-income countries range from 6 - 29%;[8-11] however, high-risk populations tend to yield higher rates of PRA.[9] Among a sample of pregnant women from Tanzania (a low-income country [12]), in the city of Mwanza, the rate of PRA was 18.3%, which was associated with antenatal depression (odds ratio 1.36, 95% confidence interval 1.23 to 1.5).[13, Rwakarema 2013 unpublished] In the lower-middle income country of India,[12] in the city of Kerala, prevalence of severe PRA ranged from 0.4% to 22% depending on the trimester, but at least 74% of Indian women experienced "moderate levels" of PRA in all trimesters which was not operationally defined.[14] Prevalence of PRA varies in part due to methodological heterogeneity (e.g., characteristics of sample, timing of measurement), and clinical heterogeneity (e.g., measuring anxiety during pregnancy rather than PRA[14]).

Within high-income countries, non-Caucasian ethnicity, low family income, and limited social supports are consistently noted as prominent risk factors for PRA.[2, 15, 16] In low-and-middle-

income countries (LMIC), it is unknown if these remain the most prominent risk factors for PRA. In Tanzania, 67% of the population falls below the poverty line and 99% of Tanzanians are of African ethnicity.[17] Moreover, 69% of the population lives in rural areas and there are only three physicians per 100000 people [17] which may result in concerns related to healthcare resources which further contributes to the potential for PRA. As such, it seems reasonable to anticipate PRA prevalence in low- and middle-income countries such as Tanzania may be comparable to PRA rates in high-risk populations within high-income countries.

Unfortunately, there is a dearth of literature examining PRA in LMIC; only 8% of LMIC are represented in literature regarding all common mental illness during the prenatal period.[18] This lack of contextually relevant literature makes it difficult to develop practice guidelines or protocols to address PRA in these countries. Moreover, in many LMIC like Tanzania, many women come from similar socioeconomic backgrounds and it remains unclear why some women develop severe PRA and others do not. Alternative theories of stress can offer insight about stressful events, such as PRA, in unexamined populations. Lazarus and Folkman [19] suggest that stress occurs when people are faced with a situation they deem a possible threat and cannot access the resources required to manage the threat. In accordance with this theory, the differences in sociocultural context between high-income countries and LMIC may be that LMIC hold different risk factors for PRA than high-income countries. Differences in countries' public health education may alter the amount of anxiety women have about the physical symptoms of pregnancy as they are more or less aware of what to expect and what is normal.[20] Moreover, difference in accessibility to health care services can affect women's appraisal of whether or not adequate prenatal care is attainable. This doubt can increase concerns about pregnancy

complications, delivery, or infant care, particularly if access to healthcare is limited or women have had previous negative healthcare experiences.[2] Consequently, factors associated with PRA in high-income countries should not be assumed true for LMIC.

We used the Social Ecology Model for Health Promotion [21] to identify predictive factors. The Model proposes health promotion is most effective when we consider the interaction of peoples' attributes and both their physical environment and social climate.[21] As people change their environment it will contribute to their change in health. In this model, the notion of "environment" is multidimensional and can include tangible attributes (i.e. upsetting events in the community) or social constructs, objective qualities or perceived qualities, and/or social climate or physical surroundings.[21] Additionally, the Social Ecology Model for Health Promotion asserts that human-environment interactions should be considered on both small and large scales (e.g. individuals, families, communities, and populations).[21] Therefore, in order to thoroughly examine factors associated with PRA in women in the low-income country of Tanzania, we examine attributes of pregnant women, their families, their communities and their environment. We sought to answer the research question: what predictive factors are associated with PRA for women attending antenatal clinics in the Ilemela and Nyamagana districts of Tanzania, Africa.

METHODS

Study design

We used data collected during women's first attendance at prenatal clinic (gestational age 6-32 weeks). These women were enrolled in a prospective longitudinal study that explored the

relationship between psychosocial health and preterm birth among women in Mwanza, Tanzania.[Premji 2013 unpublished] A collaborative research team comprised of faculty and graduate students, from University of Calgary and Catholic University of Health and Allied Sciences (CUHAS) in Mwanza, Tanzania and local registered nurses who also served as field workers, collected data at four time points throughout participants' pregnancies (first trimester, early second trimester, late second trimester, and early third trimester). During the first time point, women were coached to return to the clinic every six weeks until 32 weeks gestation, then were seen at delivery and again 6 weeks postpartum.[Premji 2013 unpublished] At each point of contact participants received a perinatal mental health assessment; private space was provided to complete questionnaires.[Premji 2013 unpublished] The Conjoint Health Research Ethics Board at the University of Calgary (approval numbers REB 13-0399 and 16-1579), and the Catholic University of Health and Allied Sciences/Bugando Medical Centre Research Ethical Committee (CREC/062/2013) approved these studies (i.e., primary and secondary analysis). The larger study was also approved by the Tanzania National Institute of Medical Research - Lake Zone Institutional Review Board (MR/53/100/254 and MR/53/100/160).

Patient involvement

Patients and/or public were not involved in the design of the study.

Setting and participants

A convenience sample of 212 women was recruited, using a systematic sampling approach, from antenatal clinics in the Ilemela (n=72) and Nyamagana (n=140) districts of Tanzania from June 2013-January 2015.[Premji 2013 unpublished] The sample was comprised of women who spoke

Swahili or English, and were 32 weeks' gestational age or less at the time of enrollment based on women's last menstrual period. Adolescent mothers were included as they were classified as emancipated minors.[Premji 2013 unpublished] Women who self-reported co-morbidities such as hypertension, diabetes, malaria or human-immunodeficiency virus (HIV) were not excluded due to the prevalence of these illnesses. Recent work within this sample revealed that the high prevalence of HIV coupled with minimal health knowledge has resulted in women with and without HIV sharing similar concerns about the illness and potential effects on their baby.[20] The nurse in-charge was the first to approach and invite participation from eligible women in the waiting room of the antenatal clinics. A member of the research team then obtained informed consent from women who agreed to participate (see image file for Figure 1 Recruitment flow diagram).[Premji 2013 unpublished]

Data collection

A general questionnaire was used to collect socio-demographic data including age, education, income, and co-morbidities.[Premji 2013 unpublished] PRA was measured using a revised version of the 10-item PRA Questionnaire (PRA-Q) that assesses feelings about health during pregnancy, infant or baby's health, and labour and delivery.[22, 23] Each item was a 4-point Likert scale of 0-3; a cumulative score was given out of a possible 30 points.[22] Information on household incomes was difficult to obtain due to cultural norms and traditions.[13] Consequently, socio-economic welfare was assessed using a Likert scale questionnaire focused on the acquisition of assets (e.g. car, motorcycle, bicycle), living standards (e.g., access to water, and number of meals eaten per day), and other wealth status (e.g., employment).[13, 24] Most questions were dichotomous (yes or no) with an associated score of one or two with the

exception of three questions; roof type and meals per day provided three possible answers with associated scores of one to three and water source had five possible answers with scores from one to five. The final score on the Socio-Economic Welfare Questionnaire (SEW-Q) was a sum of all the answers for a maximum possible score of 29. Social support was rated using the 12-item Multidimensional Scale of Perceived Social Support.[25] This scale includes questions about the relationship of supportive people to the participant, the perceived level of support the participant receives from her support network, and the extent to which the participant feels cared for by the people closest to her.[25] This scale has high internal consistency reliability (Cronbach's $\alpha > 0.90$). Perceived stress (PS) was measured with a 10-item tool (4-point Likert scale) examining the frequency of increased stress, perceived level of control over their life and stressful events, and ability to cope with stress. A cumulate score was given out of a possible 40 with higher scores indicating increased stress.[26] Evaluation of the PS scale has consistently shown adequate reliability (Cronbach's $\alpha > 0.70$) and has been used with a variety of populations and translated into 25 languages.[27] However, empirical evaluation has not been completed on these translated versions or with populations other than college students or the employed.[27] The Edinburgh Postnatal Depression Scale (EPDS), a self-reported 10-item scale was used to screen for depression and identify at-risk mothers. Empirical evaluation demonstrates good reliability (Cronbach's $\alpha=0.83$) [28]. This scale has been extensively tested in both pregnant and postnatal populations and is widely accepted for global populations with translations in several languages.[29, 30] The EPDS has been used and tested in various African countries and translated into many languages including Swahili.[31, 32]

Statistical analysis

For bivariate analysis, variables of interests (Table 1) were selected based on factors identified in the current literature, the theory of cognitive appraisal,[19] and the social ecological model for health promotion.[21] Bivariate analyses identified which continuous variables had a relationship with the PRA total score. Nominal variables with more than two values (i.e. marital status, occupation) were converted into dichotomous variables (i.e. in relationship or not) and analyzed with Mann-Whitney U tests as PRA was not normally distributed. Converted variables found to have a significant association with PRA total score were then expanded and each variable's

Table 1. Variable selected for bivariate analysis

Individual	Family	Community
EPDS Score *	Sum of SEW-Q Score *	Events in the Community Upsetting to You
Age of participant	Gravidity	Perceived Social Support Score
Mother Born in Mwanza	Current Marital Status **	Healthcare Facility
Mother's highest level education	Mother's Main Occupation	
PS Score *	Father's Main Occupation	
History of Hypertension	Father's Highest Level of Education *	
History of Depression *	Total Number of Pregnancies	
History of Gestational Diabetes	Total Number of Live Births	
History of Schistosomiasis	Previously Had Preterm *	
History of Syphilis	Previously Had a Male Baby	
History of HIV *	Number of People Living in the Home *	
History of Malaria	Planned Pregnancy *	
History of Anemia	Gestational Age at First Visit	

EPDS, Edinburgh Postnatal Depression Scale; PS, perceived stress; HIV, human-immunodeficiency virus; SEW-Q, Socio-Economic Welfare Questionnaire.
*Predictor variable in regression analysis
**Married and Separated were dichotomized predictor variables in regression analysis

original values (i.e. coupled, married, common-law, divorced, etc.) were analyzed as separate dichotomous variables using Mann-Whitney U test for an association with PRA total score.

Ordinal variables (i.e. education) were analyzed with Kruzkal-Wallis tests as PRA was not normally distributed. Variables with a significance level of $p \leq 0.25$ in the bivariate analyses were included in the multiple linear regression analyses.[33] Variables known to have clinical relevance such as socio-economic welfare score and marital status were also included regardless of their statistical significance.

Multiple linear regression modeling was employed with PRA total score as the dependent variable. In order to assess variables associated with the most severe cases of PRA, PRA scores were divided into quartiles and only cases with PRA scores in the top and bottom quartiles were analyzed in this multiple regression analyses. Given the rigorous variable selection process, a backwards input method was used. Variables were then removed starting with the variables that were least statistical significant. A two-sided p value of ≤ 0.05 was considered statistically significant for all multiple linear regression analyses. Residual of error values were then examined in a scatter plot, Q-Q plot, and histogram to verify the assumptions of normal distribution and homoscedasticity were satisfied.

We conducted supplemental analyses to provide a comparison with the primary analyses which only used cases with PRA scores in the first and fourth quartile. The first supplemental analysis employed the same multiple linear regression process as the primary analysis but included all PRA scores. We employed the same variable selection method described in the primary analysis. Currently there is no empirically tested, or commonly accepted, method for operationalizing PRA-Q scores into levels of severity. Thus, our primary analysis maintained rigor by leaving these scores as a continuous variable. To evaluate how our results may compare to studies that

have categorized PRA scores, we completed a second supplemental analysis. Using all 212 cases, PRA scores were dichotomized in accordance with the work of Fairlie et al.;[34] high-anxiety was defined as three or more answers of "3" (very much) on the PRA-Q. All other scores were categorized as low-moderate anxiety. Bivariate and χ^2 tests were conducted where appropriate, to identify factors associated with high, or low-moderate PRA.

RESULTS

The sample was comprised of 72 women from the Ilemela district and 140 women from the health center in Nyamagana (*N*=212) with a median age of 26 years (range 16 – 44 years). Approximately three-quarters of participants (78.2%) were multiparous, the majority of participants were in a relationship (89.6%), and over three-quarters of participants (77.8%) identified that they were married. Although nearly all participants (97.2%) had some level of formal education, most had only completed primary school (64.6%). Socio-economic status was higher than expected with 57.1% of participants scoring 12 or better (out of 18) on the SEW-Q and 9.0% scoring five or less. PRA-Q scores ranged from 0-24 with a median score of 10 (inter quartile range (IQR)=8-13). When PRA was dichotomized as "high" and "low-moderate" categories, 6.1% of participants (n=13) had high anxiety. Table 2 shows the demographic characteristics and PRA scores of the study's sample.

Table 2. Demographic characteristics

	Total N=212	Nyamagana n=140 (66%)	Ilemela n=72 (34%)
	Median (range)	Median (range)	Median (range)
Age (years)	26 (16-44)	33 (16-44)	29 (17-40)
GA (weeks) at 1st visit	24 (6-32)	23 (6-32)	26 (8-32)
	N (%)	n (%)	n (%)

Primiparous	50 (21.8)	33 (21.6)	17 (22.7)
Born in Mwanza	71 (33.5)	52 (37.1)	19 (26.4)
Primary Education	137 (64.2)	104 (74.3)	33 (45.8)
> Primary Education	69 (32.5)	33 (23.6)	36 (50.0)
Married	165 (77.8)	105 (75.0)	60 (85.7)
Employed	138 (60.3)	92 (60.1)	46 (61.3)
	Median (range)	Median (range)	Median (range)
Sum of SEWQ Scores	12 (2-18)	12 (2-18)	13 (2-16)
Perceived Social Support Score	59 (20-84)	59 (21-84)	59 (20-80)
Perceived Stress Score	19 (1-36)	18 (1-36)	21 (8-33)
EPDS	8 (0-26)	7 (0-25)	9 (0-26)
PRA-Q total Score	10 (0-24)	10 (0-24)	12 (2-24)

GA, gestational age; PS, perceived stress; SEW-Q, Socio-Economic Welfare Questionnaire; EDPS, Edinburgh Postnatal Depression Scale; PRA-Q, Pregnancy-Related Anxiety Questionnaire

In the primary analysis, PRA scores were quartiled and only cases from the first and fourth quartile were used (n=90). The first quartile scores ranged from 0-7 and the fourth quartile scores ranged from 13-24. The variables included in the multiple linear regression analyses are shown in Table 1. The results of the primary regression (Table 3) indicated that PS score, EPDS score, and number of people living in the home were significant predictors of PRA (R^2=0.339, $F(3,74)$=12.657, p=0.000) (adjusted R^2=0.312). PS score and EPDS score were positively associated with PRA score, whereas the number of people living in the home was negatively associated with PRA score. There was no indication of multicollinearity as each of these predictors met the criteria for statistical significance ($p \leq 0.05$), had a Variance Inflation Factor of less than 2, and a Tolerance greater than 0.05. While the EPDS is supposed to measure postpartum depression, there is concern the scale contains an anxiety subscale.[35] To account for a potential spurious relationship between this anxiety subscale and PRA, the EPDS scores were recalculated, excluding the scores for two anxiety-related questions. Bivariate analysis indicated the recalculated EPDS scores and full EPDS scored shared the same correlation with PRA score (r_s=0.511, p=0.000). When the linear regression modeling was re-run using the

recalculated EPDS scores the model summary was only marginally changed (R^2=0.338, F(3,74)=2.607, p=0.000) (adjusted R^2=0.311). The total of the two anxiety questions from the EPDS was analyzed as a separate variable. This variable showed a positive correlation with PRA scores (r_s=0.422, p=0.000) but was not a statistically significant predictor in the regression models.

Table 3. Regression model of factors associated with PRA score

	B	*SE B*	β	*t*	*p*
PS Score	0.306	0.121	0.328	2.527	0.014
EPDS Score	0.328	0.136	0.316	2.416	0.018
Number of people living in home	-0.718	0.342	-0.204	-2.102	0.039

PS, perceived stress; EDPS, Edinburgh Postnatal Depression Scale

In the first supplemental analysis (using all cases, n=212), PRA had a significant association (p≤01.05) with EPDS score, recalculated EPDS score, PS, SEW-Q score, a history of HIV, and healthcare facility. The results of this regression analysis were similar to the regression modeling using the first and fourth quartile PRA scores; results indicated PS score and EPDS score were statistically significant predictors of PRA (R^2=0.196, F (2,209)=25.394, p=0.000) (adjusted R^2=0.188). Both PS score and EPDS score maintained a positive correlation with PRA. This regression was re-run using the recalculated EPDS scores and the model summary was again only marginally different (R^2=0.195, F(2,209)=25.243, p=0.000) (adjusted R^2=0.187) with the same final predictors.

In the second supplemental bivariate analysis with dichotomized PRA, the number of people living in the home, PS score, and EPDS scores showed significant associations (p≤0.05) with high or low-moderate PRA. Fisher's Exact test showed PRA to have a significant association with if the mom was born in Mwanza, and if the pregnancy was planned. Eighty-five percent

(*n*=11) of the participants with high anxiety had not planned their pregnancy. X^2 analysis showed presence of depression (an EPDS score of 13 or higher [29]) was two-fold in women with a high PRA scores (53.8%) compared to women with low PRA scores (27.1%) (*p*=0.04). When EPDS scores were recalculated without the anxiety questions, the presence of depression remained about two-fold in women with high PRA scores compared to women with low PRA scores (23.1% and 11.6% respectively). However, these results were not statistically significant (*p*=0.203).

DISCUSSION

Twenty-five percent of women in our sample scored 13 or higher (out of a possible 30) on the PRA-Q, and 6.1% of participants met the threshold for "high anxiety".[34] Regardless of how PRA was operationalized (continuous, dichotomized, or limited to only the highest and lowest scores), EPDS score and PS score consistently had a positive correlation with PRA and were significant predictors in the regression models. Current literature substantiates the identified association between depression and PRA.[1, 13] Pregnant women more commonly experience co-morbid anxiety and depression rather than one of these afflictions alone.[13, 36] However, there appears to be limited understanding of why this comorbidity exists and which develops first, depression or anxiety. Consideration of the Theory of Stress, Appraisal, and Coping [19] combined with the nuances of this sample's cultural context provides insight in this inquiry. Lazarus and Folkman [19] posit that stress results when an event is appraised as a possible threat to one's well-being and the resources to mitigate the event are deemed unattainable. Moreover, factors such as novelty and time proximity to the event can affect the perception of the threat's severity.[19] In accordance with this theory, the lack of basic health knowledge, coupled with

restricted access to healthcare facilities, and the low socio-economic standing of most Tanzanians creates an environment where pregnancy could commonly result in stress or anxiety.[17, 20] Moreover, social customs in Tanzania deter the discussion of personal matters with anyone: friends, family, or spouses.[20] A phenomenological study used a subsample of our participants to explore moderate to severe PRA. This study identified common feelings of isolation and alienation amongst participants as their anxiety worsened and there was no perceived acceptable forum to discuss their fears; ultimately, women endorsed the isolation evolving into sadness.[20, 37] Even in cases where women surrounded themselves with family, there was still a reluctance to discuss their concerns. Our primary analysis revealed a negative correlation between number of people living in the home and PRA. More people in the home increases the likelihood that the mother has someone she may feel comfortable talking to. It is therefore conceivable that in this populace, severe PRA may trigger an internal conflict of wanting to express these fears while worrying that this is not acceptable, which results in feelings of isolation and subsequent depression.

Interestingly, the factors most commonly associated with PRA in current literature did not hold significance in this study. Socio-economic welfare score showed a significant correlation with PRA only when all participants were used and PRA was a continuous variable. When PRA scores were dichotomized or only participants with the PRA scores in the first and fourth quartile were used, the correlation with socio-economic welfare score lost statistical significance, and did not show significant predictive properties. Perceived social support score, marital status, and mother's occupation also failed to have a significant association. Active depression is the only factor found to predict PRA in our study which is also consistently correlated to PRA in current

literature.[1, 13] Our findings are remarkably contrary to the current literature, which consistently lists social supports, ethnicity, and economic status as key risk factors.[2, 15, 16] Our findings serve as a caution to generalize findings on PRA from high-income countries to populations in LMIC. These gross variations from current research may reflect the limited research available from LMIC.[18]

We identified only two studies (each with two articles), one from India and the other from Tanzania, which used the pregnancy-specific anxiety inventory [14, 38] and PRA-Q [13, Rwakarema 2013 unpublished] to measure PRA, respectively. In the India study, younger age and not living with extended family were associated with higher PRA.[14, 38] Comparatively, results of the current study found no statistically significant relationship with the mothers' age in any of the analyses (primary or secondary). Number of people living in the home was not statistically significant in either analysis where PRA was maintained as a continuous variable (primary or first supplemental). When PRA was dichotomized, however, number of people living in the home showed statistically significant negative correlation with PRA. The nature of relationship between the mother and people living in the home was not examined in the current study thus comparison between our study and the India study is difficult. In the Tanzanian study, PRA was noted to have a statistically significant relationship with prenatal depression.[13, Rwakarema 2013 unpublished] The Tanzanian study was examining factors associated with antenatal depression, consequently the underlying aim of the study was different (i.e., clinical heterogeneity).

Despite the vast differences in culture and socioeconomic standing it makes sense that globally, women can experience the same condition, PRA, for different reasons. Pregnancy and childbirth have high-risk of death for the mother and baby in Tanzania.[39] The neonatal mortality rate is about 26 for every 1000 lives births and the maternal mortality rate of 398-454 for every 100000 lives births.[39] In the previously mentioned phenomenological study, fears about health during pregnancy was a commonly noted factor contributing to PRA.[20, 37] High likelihood of death may be an unfortunate reality for populations in LMIC resulting in a fear of death having a greater effect on overall PRA than in women from high-income counties. With the multidimensional nature of PRA, women may assign greater emphasis on different domains of PRA based on issues most relevant for their cultural context.[40]

The notion of novelty can critically change the perceived threat in an event.[19] Pregnancy may be uniquely novel in its accompaniment of physiological and psychological emotional investment coupled with the distinct outcome of creating human life. One possible explanation is that pregnancy may hold an unparalleled element of novelty (thus propensity to induce anxiety) regardless of a women's background or gravidity. Differences in social norms and fundamental values, however, may change what someone considers threatening or stressful.[19] In the context of this study, socio-cultural norms such as dynamics between men and women may change the effect of social supports on PRA scores. The subsample of women enrolled in the phenomenological study of PRA often described their husbands growing distant during the pregnancy, which had an exacerbating effect on their anxiety rather than calming.[20] Many of the fears voiced by women in Tanzania were due to limited basic health and pregnancy knowledge; many times normal sensations resulted in fear of death for the mother or baby.[20]

These differences in findings outline the need for more research exploring the notion of PRA in LMIC and between LMIC and high-income countries.

Limitations

Convenience sampling was employed and consequently results cannot be generalized to all pregnant women in the Ilemela and Nyamagana districts of Tanzania. Moreover, the lack of comparable studies in LMIC makes it difficult to identify potential anomalies in these findings. There are no standardized screening tools for PRA or commonly accepted categorization methods for the tools available [40] making it difficult to compare findings between studies or compare characteristics between levels of severity of PRA. Moreover, within current literature there is no empirically tested way to operationalize PRA scores. The PRA-Q examines broad concepts of PRA making it an effective screening tool but difficult to identify severity of PRA or clinical diagnoses.[40, 41] This was a secondary data analysis limiting variable options to those already included in the longitudinal study. Findings in the regression modeling only explain 20-34% of the change in PRA scores across our sample. Consequently, there are still significant factors not identified in this study.

CONCLUSION

Active depression is one of the only factors consistently correlated to PRA in both our study and current literature. Given the socio-cultural differences between populations in high-income countries and LMIC, the unique psychological complexities of pregnancy, and the personal nature of how people assess events as stressful, findings should not be generalized across these populations. Ultimately, more research is needed on PRA universally and the reason for

comorbidity between depression and PRA. In LMIC, before predictive factors and prevention strategies can be identified, further fundamental exploration of PRA is needed to better understand how this phenomenon fits within these socio-cultural settings.

Contributions: VW, and SSP worked together to develop the research question, study design, and analytic plan. SSP, NL and GM provided consultation from the research design through to the manuscript development, and directed the analysis of the study. ECN, local lead in Mwanza, translated documents, obtained ethics approval, and supervised research assistants. All authors have contributed to the work and approved the manuscript.

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Competing interests: None declared

Ethics approval: University of Calgary Conjoint Health Research Ethics Board (REB13-0399: larger study; REB14-0660: this study; and REB14-0660-MOD-1: to include postpartum women) and the Catholic University of Health and Allied Sciences.

Data sharing statement: The dataset generated during our study are not publicly available as consent for secondary use was not obtained from study participants. Please contact the corresponding author for additional information.

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LEGEND

Tables

- Table 1. Variable selected for bivariate analysis
- Table 2. Demographic characteristics
- Table 3. Regression model of factors associated with PRA score

Figures

- Figure 1. Recruitment flow diagram

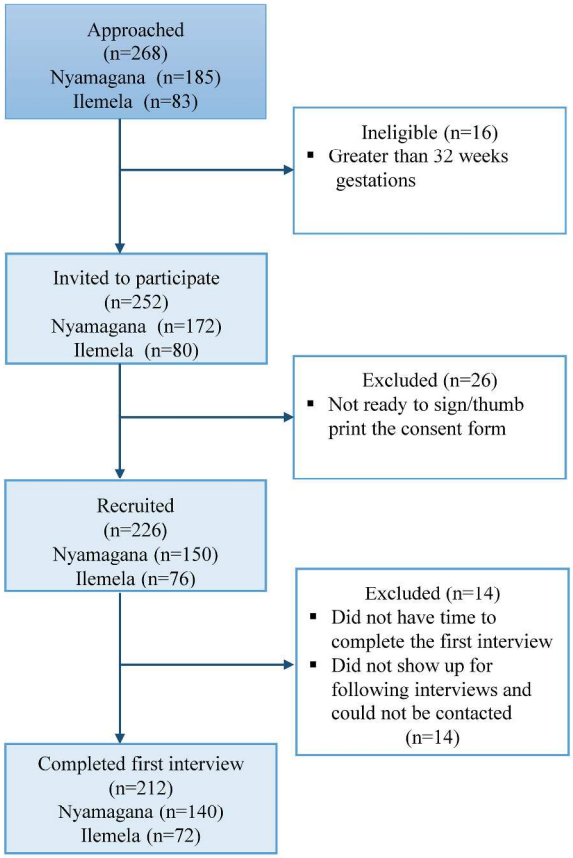

Figure 1. Recruitment flow diagram

254x338mm (300 x 300 DPI)

STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1-2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-6
Objectives	3	State specific objectives, including any pre-specified hypotheses	6
Methods			
Study design	4	Present key elements of study design early in the paper	6-7
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	7-8
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	7-8
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	N/A
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	8-10
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	8-9
Bias	9	Describe any efforts to address potential sources of bias ***(systematic sampling to reduce selection bias)***	7
Study size	10	Explain how the study size was arrived at ***(convenience sample)***	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	9-10
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	9-11
		(*b*) Describe any methods used to examine subgroups and interactions	11
		(*c*) Explain how missing data were addressed	N/A
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	N/A

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses ***(supplemental analyses conducted)***	11
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	12
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	12
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	12-13
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	12-14
		(*b*) Report category boundaries when continuous variables were categorized	12-13
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	14
Discussion			
Key results	18	Summarise key results with reference to study objectives	14-17
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	17
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	18
Generalisability	21	Discuss the generalisability (external validity) of the study results	17
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	18

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.