

Prevalence And Factors Associated With Depression Among Adults With Sickle Cell Disease at Mulago Hospital, Uganda: a Cross Sectional Study

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Abstract

BACKGROUND

Depression among patients with sickle cell disease (SCD) is under diagnosed and undertreated due to the overlap of symptoms and signs of SCD and depression. The study sought to determine the prevalence and factors associated with depression among adults attending the SCD out-patient clinic in Mulago Hospital, Uganda.

METHODS

This was a cross sectional study in which 255 adults with SCD were enrolled. Participants were evaluated for depression using the Self Report Questionnaire (SRQ-20) and a score of 6 was considered diagnostic of depression. Demographic data was collected with a pre-tested study questionnaire. Perceived social support was measured using the 12-item multidimensional social support scale and, self-esteem was measured using the Rosenberg Self-Esteem Scale. Blood samples were taken to obtain a complete blood count. Modified poisson regression analyses were used to determine associations of depression.

RESULTS

The prevalence of depression was 68.2% (95% C.I; 62–74) with a median age of 21 years. The factors independently associated with depression were pain crisis in the last month (prevalence ratio (PR) = 1.07, 95% CI: 1.04–1.07, $p = 0.001$), history of a hospital admission in the past 6 months (PR = 1.04, 95% CI: 1.01–1.07, $p = 0.012$), formal education (PR = 0.79, 95% CI: 0.59–0.97, $P = 0.008$) and a low social support rating (PR = 0.67, 95% CI: 0.53–0.84, $P = 0.0019$)

CONCLUSIONS

The prevalence of depression in adults with SCD is high with up to two thirds of patients having some form of depression. The major risk factors were low level of education, low social support, pain crises in the past month and hospital admissions in the last 6 months.

Background

Sickle Cell Disease (SCD) is the most common genetic haematological disorder(1). Approximately 235,000 babies with sickle cell disease (SCD) are born each year worldwide (2). It accounts for 6.4% of the under-5 mortality across all of Africa (3).

SCD is one of the most common genetic disorders in Uganda, and has life-long implications for those afflicted with it. SCD affects approximately 0.7% of the Ugandan population (3). It affects close to

200,000 Ugandans many of whom lack access to adequate clinical management services and as such are frequently plagued by complications like recurrent vaso-occlusive crises and infections (4).

SCD may result in significant morbidity, as well as increased mortality(1). Patients with SCD have a life-long, often severe anaemia, frequent vaso-occlusive crises and develop complications such as acute chest syndrome, infections, strokes, seizures, priapism, fat embolization, pulmonary hypertension, thrombosis, retinopathy, renal failure, gallstones, liver disease and bone infarctions (2). There is considerable variability in the clinical course of SCD with some patients experiencing few to no complications while others present with multi-system complications (2).

Studies suggest that Depression in SCD is highly prevalent in Low income settings with a prevalence of 21.6% in a study among adults living with SCD in Jamaica (5).

Depression and loneliness may exist in those with chronic diseases, but the coexistence of depression in people with SCD in low resource settings is not well elucidated. Depression is a mood disorder marked especially by sadness, inactivity, difficulty in thinking and concentration, a significant increase or decrease in appetite and time spent sleeping, feelings of dejection and hopelessness, and sometimes suicidal tendencies.

Some studies have demonstrated that depression may worsen clinical outcomes in patients with chronic illnesses (6). Among those with SCD, this could lead to poor treatment adherence, missed clinic appointments and increased admissions which in turn pose a greater financial and social burden both for the patient, their caretakers as well as the national health budget (7).

Depression was found to be a significant factor associated with hospital admissions in persons living with SCD who were attending the Mulago hospital clinic irrespective of sex and income. It was found to significantly increase hospital admissions over a one year period (8).

Only a few studies have looked at the prevalence of depression in SCD and its impact on clinical outcomes in sub-Saharan Africa. A small study of 38 patients with SCD and 38 controls in Nigeria found that SCD patients and matched controls differed significantly on both the physical and mental illness scores. This study demonstrated that anxiety and depression were 3 times more common among the SCD patients than the controls (9).

There is a paucity of studies that have evaluated the prevalence of depression in SCD and the factors associated with depression in SCD in resource limited settings. Complications of SCD compounded with social factors attributed to living in low income settings may increase the risk of depression among patients with SCD.

In spite of this, the prevalence of depression among patients of SCD in Uganda has not been studied and this creates a vital research area that would be relevant in informing the national sickle cell management guidelines.

The aim of this study was to determine the prevalence of depression and factors associated with depression among adults attending the SCD out-patient clinic in Mulago Hospital, Uganda.

Methods

Study population and settings

This was a cross sectional study that aimed at determining the prevalence and the factors associated with depression in SCD in adult patients attending the Mulago sickle cell clinic. Mulago hospital is one of only two national referral hospitals in Uganda and is located in Kampala city, the capital city of Uganda. The Mulago sickle cell clinic serves as the centre of care for people living with SCD to which all other units of the hospital and peripheral facilities in Kampala district refer patients for diagnosis and treatment. The clinic manages up to 7000 registered patients attending scheduled visits on weekdays for clinical review and outpatient treatment. .

Individuals with Sickle cell disease were recruited in the study if they were aged 18 years or above, provided written informed consent, and could speak either English or *Luganda* -the local language spoken in central Uganda where the study site is located. Individuals with Sickle cell disease who were critically ill as indicated by a score of ≤ 30 on the Karnofsky performance scale were excluded from the study.

On each clinic day, the attendance register was obtained and every third individual on the register was assessed for study eligibility.

Sample size estimation

Using the prevalence of depression in SCD of 21.6% in a clinical setting in Jamaica in 2010(5), with the accepted absolute error of 0.05; the sample size was estimated to be 260

Data Analysis

Statistical analysis was carried out with STATA, version 13. Frequencies of participant's characteristics were computed. Numerical data were summarised using means and standard deviation for normally distributed data or medians and interquartile ranges for continuous but skewed variables. Logistic regression analyses were conducted to determine associations which socio-demographic characteristics, clinical variables and psychosocial characteristics were associated with depression defined as a cut-off score of 6 and above on the SRQ-20. For the bivariate analyses, we used Chi-square tests or Fisher's exact test for categorical variables, and independent-sample t tests for continuous variables. Variables that had a significant bivariate association with depression symptoms were then included in a multi-variate logistic regression model using stepwise regression and the modified Poisson regression method to determine the factors independently associated with depression. Data was collated using frequency tables and figures. A p-value of ≤ 0.05 was considered statistically significant.

Study measures

Research assistants administered pre-tested study questionnaire that sought for sociodemographic and clinical variables to eligible participants. We further interrogated participants' clinical records and determined whether the individual had history of a stroke in the past, leg ulcers in the past six months and painful crises in the past month. Study participants were examined for leg ulcers and blood samples were drawn to determine the haemoglobin level from the complete blood count.

Depression was assessed with the Self-Reporting questionnaire (SRQ-20). Individuals who scored a score of 6 or above were regarded as having depression. The SRQ-20 is a 20-item questionnaire used to screen for psychological distress. It scores from arrange of 0 to 20 with higher scores correlating to increased psychological distress. However, a psychometric evaluation using this questionnaire among Persons living with HIV (PLWH) indicated that those individuals who scored a score of 6 or above had an 89% chance of meeting diagnostic criteria of major depression (10).

Perceived social support was assessed using the 12-item multidimensional social support scale(MSPSS) (Appendix 3), which provides assessment of three sources of support: family (FA), friends (FR), and significant other (SO) (11). The scale has been validated in Uganda and the three-subscale structure (Family, Friends, and Significant Other) of the MSPSS was consistently observed (12). The Cronbach α for this sample was 0.94. Responses were based on a 7-point likert scale where 1–4 referred to those who very strongly, strongly, mildly disagreed and those who were neutral about having enough support from friends, family and significant others respectively. Scores of 5–7 referred to those who mildly, strongly or very strongly agreed to have enough support respectively. Individuals with a mean score of 3 or less were regarded as having low social support, those with a mean score of 4 to 5- moderate social support and those with a score of 6 or more – high social support.

Self-esteem was assessed using the Rosenberg Self-Esteem Scale (13) .It provides assessment of one's general feelings about oneself. This is a 10- item Likert scale with items such as, "On the whole, I am satisfied with myself"; "I feel that I have a number of good qualities". Responses were based on a 4-point scale where 1–4 referred to those who responded with "I strongly agree", "I agree", "I disagree" and "I strongly disagree" respectively. A total score below 15 suggests low self-esteem. This scale has been used in HIV positive women in South Africa (14).

Results

Between November 2017 and February 2018 we enrolled 260 study participants. Of the 260 patients enrolled, 5 were not included in the analysis because they were unsure of their ages.

Prevalence of depression

Of the 255 study participants who then remained, 174 (68.2%, 95% C.I: 62–74) met the criteria of depression as defined by the SRQ-20.

The mean SRQ score was 8 (SD = 4.57).

The majority of study participants (63.14%) were female and the median (Interquartile Range (IQR)) age of all the participants was 21 (19–25) years. The mean haemoglobin for the entire study population was 8.2 g/dl (SD = 1.76) with 6.54% of the total study participants having no anaemia or mild anaemia (defined by Hb 11–13 g/dl), 85.38% having moderate anaemia (Hb 6–11 g/dl) and 8.08% having severe anaemia (Hb < 6 g/dl). The mean MCV was 78.4 (SD = 10.18) fl.

Other baseline characteristics are shown in the Table 1

Table 1
Baseline characteristics of the adults attending the sickle cell clinic, Mulago hospital, February 2018

Characteristic	Total N = 255
Male n(%)	94 (36.9%)
Age (Median, IQR)	21(6)
Region of ancestral Origin, n (%)	192(75.3%)
Central Eastern	43(16.9%)
Eastern	9(3.5%)
Western	11(4.3%)
Northern	
Marital Status, n (%)	232(91%)
Single	21(8.2%)
Married	2(0.8%)
Divorced	
Unemployed	52(20.4%)
Education status	2(0.8%)
No formal education	58(22.8%)
Formal education	

Table 2
Psychosocial ratings of the study participants in Mulago Kampala,

SOCIAL SUPPORT	22(8.7%)
Low social support	116(46.0%)
Moderate social support	114(45.3%)
High social support	
SELF ESTEEM	12(4.7%)
Low esteem	243(95.3%)
High esteem	

Table 3
Clinical characteristics of the study participants in Mulago Kampala,

History of Stroke, n (%)	26(10.3%)
Leg ulcers, n(%)	38(15%)
Family history of mental illness, n(%)	58(22.9%)
Painful crises in last month, n(%)	152(60.0%)
HAEMOGLOBIN	8.2(1.7)
Hb mean (SD)	17(6.5%)
Mild anaemia (Hb 11–13 g/dl)	222(85.4%)
Moderate anaemia(Hb 11 – 6 g/dl)	21(8.1%)
Severe anaemia (< 6 g/dl)	

We compared the clinical characteristics of the two sub groups (patients diagnosed with depression and those with no depression). We found 12.7% of those diagnosed with depression reported a history of stroke while only 5% of the study participants who did not have depression reported a history of stroke. Among the males, 6.2% of those diagnosed with depression reported suffering from priapism in the last six months compared to 8.7% in those who did not have depression ($P = 0.507$).

Leg ulcers were found in 17.3% of the depressed group compared to 10% of those who were not depressed ($P = 0.129$). There was a similar proportion that reported a family history of mental illness between the two groups with 17.3% of the depressed having a positive family history of mental illness while those who were not depressed had 17.5% with a positive family history.

There was a significant difference between the number of hospital admissions among participants diagnosed with depression and those with no depression ($P = 0.012$). In addition, 80% of participants with

depression reported having a hospital admission in the past 6 months compared to only 7.5% of those who did not have depression.

Factors associated with depression among SCD.....

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Table 4
Factors associated with depression at bivariate analysis (N = 255) in Mulago Kampala,

Variable	Depressed, n (%)	Univariate PR (95% CI)	Multi-variate PR (95% CI)	
Sex	64(36.8%)	1		
Male	110(63.20%)	1.0(0.84–1.19)		
Female				
Age	78(45.3%)	1		
18–20 years	71(41.3%)	0.99(0.82–1.19)		
20–30 years	23(13.4%)	1.14(0.89–1.45)		
> 30 years				
Religion	43(25.1%)	1		
Moslem	91(53.2%)	0.98(0.80–1.20)		
Anglican	37(21.6%)	0.99(0.77–1.27)		
Catholic				
Region of origin	129(74.1%)	1		
Central	31(17.8%)	1.07(0.87–1.33)		
Eastern	14(8%)	1.04(0.76–1.42)		
Others				
Marital status	17(9.8%)	1		
Never married	157(90.2%)	1.09(0.84–1.42)		
Ever married				
Occupation	133(76.4%)	1		
Employed	41(23.6%)	1.20(1.01–1.43)		
Unemployed				
EDUCATION	52(29.9%)	1	1	0.008
Never/Primary	88(50.6%)	0.76(0.65–0.89)	0.81(0.697–0.95)	
Secondary	34(19.5%)	0.64(0.50–0.82)	0.79(0.59–0.97)	
Tertiary				

Variable	Depressed, n (%)	Univariate PR (95% CI)	Multi-variate PR (95% CI)
History of stroke	22(12.7%)	1	
Yes	151(87.3%)	0.79(0.65–0.95)	
No			
SOCIAL SUPPORT	20(11.6%)	1	
Low support	152(88.4%)	0.59(0.48–0.74)	
Moderate-high support			
SELF ESTEEM	8(4.7%)	1	
Low Esteem	163(95.3%)		
High Esteem			
ANAEMIA	15(8.62%)	1	
No anaemia/mild	142(81.61%)	0.74(0.61–0.91)	
Moderate anaemia	17(9.77%)	0.91(0.69–1.2)	
Severe anaemia			
Pain crisis in the past month	44(54.3%)	1	
No	37(45.7%)	1.08(1.05,1.12)	
yes			
Hospital admission in past six months	75(92.5%)	1	
Not admitted	6(7.5%)	1.03(1.00,1.06)	
Admitted			

PR- prevalence ratio

Comparison of clinical factors among patients with depression and those with no depression at bivariate analysis found a significant difference in level of education ($p = 0.001$), social support rating ($p = 0.001$) self-esteem rating ($p = 0.049$), history of admission in the past six months ($p = 0.044$), and pain crisis in the past month ($p = 0.045$)

Table 3
Factors independently associated with depression among adults with SCD attending Mulago OPD.

	Multivariable analysis	
	PR (95% CI)	p-value
EDUCATION	1	0.008
Never attended /Primary	0.81(0.697–0.95)	??? (p-value)
Secondary	0.79(0.59–0.97)	
Tertiary		
SOCIAL SUPPORT	1	0.001
Low support	0.9(0.76–1.09)	???? (p-value)
Moderate support	0.67(0.53–0.84)	
High support		
Hospital Admission in past 6 months	1.04(1.01–1.07)	0.012
Pain crisis in the last month	1.07(1.04–1.10)	0.001
PR- Prevalence Ratio		

Those who achieved tertiary education (Prevalence ratio (PR) 0.79, 95% confidence interval (CI): 0.59–0.97, P = 0.008) were 21% less likely to suffer from depression compared to those who never attended school or stopped at primary school level. Those with high social support (CI: 0.53–0.84, P = 0.001) were 33% less likely to suffer from depression than those with low social support.

Study participants admitted to the hospital in the last 6 months (PR = 1.04, 95% CI: 1.01–1.07, P = 0.012) were 4% more likely to be depressed than those with no admission in the same period. The study participants who experienced a pain crisis within the last month (CI; 1.04–1.10, P = 0.001) were 7% more likely to suffer from depression than those who had not experienced a recent pain crisis.

Discussion

This study sought to determine the prevalence of depression and the factors associated with it among adults with SCD attending the Mulago hospital SCD clinic. The results show a uniquely high proportion (68.2%) of adult patients with SCD suffering from depression.

When compared to previous studies the findings of a high prevalence of depression in SCD correlate with other studies which found up to 56.5% to have varying levels of depression (8). Another study found up to 40% of patients with SCD had depression (15). In a study by Schaeffer, *et al* that included 440 patients with SCD, up to 43.4% had depression and this was more closely associated with demographics than

disease severity as measured by degree of anaemia (16). A study in Jamaica reported a slightly lower prevalence of depression in SCD (21.6%). This study population included patients with both SCD and thalassemia which may affect the disease severity (5). A study of patients living with SCD in USA found up to 20% of patients were depressed (17). The findings of this study in Mulago hospital, Uganda, generally show a much higher prevalence of depression in this group of patients than in other studies. This could be partly attributable to the effects of a lower socioeconomic environment which has been shown to increase the risk of depression (18). This study had more females, who have higher rates of depression,; however sex wasn't a predictor of depression in this study.

We found 5 patients (2%) were suicidal, however this tool has limited ability to assess suicidal tendencies and more appropriate suicide risk tools would need to be applied to confirm this. These patients were referred to the mental health clinic.

The main factors found to be associated with depression in adult patients with SCD were the social support, level of education, painful crises over the past month and hospital admissions over the past six months.

Factors relating to disease severity such as haemoglobin level and presence of leg ulcers were not found to be significantly associated with depression among patients with SCD. This is in keeping with an earlier study that showed that depression in SCD was more closely linked with demographic and psychological aspects than with disease severity(16). This has been attributed to the adverse socioeconomic difficulties that patients of SCD suffer from due to the demands of the illness such as medical healthcare costs and disability from wide ranging complications (19).

Respondents whose perception of social support was found to be positive and adequate were less likely to suffer from depression. These respondents felt that they had a special person in their lives and it was a protective factor from suffering from depression. In this study, those having moderate to high social support rating were 33% less likely to have depression compared to those with low social support.

This is in agreement with other studies which demonstrated that patients with greater social support had less depressive symptomatology and social support was seen as one of the social determinants for overall health in the general population (20). Another study looking at perception and quality of social relationships further demonstrated that good perception of social support was protective against depressive disorders (21).

The other factor associated with depression was the level of education. Respondents who had secondary level education were 18% less likely to have depression compared to those who had never studied or had stopped at primary school level. The respondents who achieved tertiary level education were even less likely to have depression with a 24% lower likelihood of having depression as compared to those with no education or just primary level education.

In this study less than a quarter of the respondents had achieved tertiary level education. This could be a reflection of the limitations in social economic status or the challenges of living with a potentially debilitating disease. There have been several studies that have looked into and demonstrated that the level of education does indeed predispose to an increased risk of depression. A study in Canada looking at depression in type 2 diabetics found that having less than 12 years of formal education was associated with a significantly increased risk of depression. These type 2 diabetes patients were 50% more likely to have depression if they had less education (22). A large study in Norway looking at prevalence and factors associated with depression in the general population found similar results with education providing a cumulative protective effect the higher along one progressed with education (23).

Hospital admission over the past 6 months was also found to be significantly associated with depression. This is in agreement with other studies that demonstrated that depression in SCD was associated with increased hospital admissions. A study among African-Americans with SCD and depression found 44% of the subjects had been treated in the emergency room more than five times in the last year which was significantly higher than those without depression (8). This could be attributed to the fact that depression compounds symptoms like pain and complicates its treatment making patients more likely to experience crises that would necessitate hospital admission. It has been shown that chronically depressed sickle cell patients displayed increased frequency of vaso-occlusive crises and other complications (24).

A pain crisis experienced within the past month was also found to be significantly associated with depression in this study. Those who had experienced a pain crisis in the past month were 7% more likely to be depressed. This could be attributable to the impact of frequent vaso-occlusive crises on the quality of life of these individuals. It could also point towards the difficulty of controlling pain in depressed patients given that pain is one of the neuro-vegetative signs that may occur in depression, and therefore, focusing on only the physical aspects is inadequate for pain control.

Similar findings of the association between pain crises and depression in SCD were demonstrated by Wallen et al who found more frequent pain crises to be the most significant associated factor with depression and sleep disturbance disorders in adult patients with SCD (17). Hasan et al also supported similar findings in his study in the USA (7). More recently a study comparing SCD patients in Jamaica with depression to controls found that more painful crises (one or more per month) was among the factors significantly associated with depression in adults with SCD (5).

There was no association between self-esteem and depression in this study ($P = 0.05$). Similar results were found in a study in Benin (25).

Although there was a high proportion of depression, we were unable to grade the severity of depression because we used the SRQ-20 which is a screening tool. Other tools such as the Beck Depression Inventory could be applied in future studies to grade the severity of depression. It is also important to note that the SRQ-20 is a screening tool which could lead to over estimation of the findings.

Some of the complications of SCD such as pulmonary hypertension and renal disease were not assessed. It was therefore not possible to determine if there was any association between these other complications of SCD and depression.

There was also a recall bias caused by differences in the accuracy or completeness of the recollections retrieved by study participants regarding events or experiences from the past, this is a methodological issue due to use of interviews or questionnaires.

Clinical Implications

There are a significant number of adults with SCD attending the Mulago OPD with depression and there are currently no guidelines for screening these patients. This evidence could serve as a guide for clinicians to determine which patients are at risk of depression (e.g. those with frequent painful crises) and enable early identification and management of these patients in order to improve on treatment outcomes. This calls for integration of mental health services in the day to day running of the clinics offering services to those living with SCD. at the sickle cell OPD to offer holistic care.

Conclusions

The prevalence of depression in adults with SCD attending the Mulago OPD was 68% and this was higher than had been described in previous studies. Depression in adults with SCD was mainly associated with more than one painful crises in the past month, low social support, low level of formal education and having hospital admission within the past 6 months.

Given these findings, it is recommended that all patients with SCD should be screened for depression especially those with a history of frequent painful crises and frequent hospital admissions. Health workers should be trained in basic mental health care to enable them screen for mental health issues in the day to day care offered to patients with SCD. Interventions to manage depression are required; this will include developing psychotherapeutic interventions for SCD that will involve the caregivers in the care. Where necessary a psychiatric team and antidepressants should be used for the individuals with moderate to severe forms of depression

Improve social support, this will entail encouraging the caretaker's to be involved in the day to day lives of people living with SCD, this will improve the perception of social support thereby protecting against depression.

Prompt and comprehensive pain management should be constituted as part of the basic healthcare package as it would both provide relief from pain and reduce hospital admissions, both of which could result in less likelihood of depression. This ranges from medications that control acute pain such as morphine to drugs that reduce likelihood of painful crises in the long-term like hydroxyurea.

Comprehensive training on pain management for healthcare workers attending to patients with SCD should also be done to ensure optimal care is provided.

Abbreviations

SCD – Sickle Cell Disease

OPD – Outpatients Department

SRQ-20 - Self Reporting Questionnaire

MPSS- Multidimensional Scale of Perceived Social Support -

Hb- Haemoglobin

MCV- Mean Corpuscular Volume

PLWH- People Living with HIV

IQR- Inter-Quartile Range

SD- Standard Deviation

Declarations

Ethical approvals and consent to participate

The study proposal was presented to the Department Of Medicine and then to the School Of Medicine Research and Ethics Committee for Institutional Review Board (IRB) for ethical approval. This cleared the study for approval by the National Council of Science and Technology. Permission to carry out the research was then obtained from the Sickle Cell Disease Clinic in Mulago Hospital. Detailed information about the study was given to the study participants and voluntary consent was sought. All those we approached were willing to participate. To ensure patient's confidentiality, unique study numbers were used in the place of their names.

Consent for Publication

Consent was received from all study investigators

Data availability statement

The datasets are available upon request from the corresponding author

Competing interests

The authors have no competing Interests to declare

Funding

None

Authors' contributions

Ivan Mubangizi- Study conception, data accrument and analysis, manuscript preparation

Ismail Kawooya- Data analysis

Etheldreda Nakimuli-Mpungu – Data analysis

Christine Sekaggya-wiltshire – study supervision, manuscript preparation

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Figures

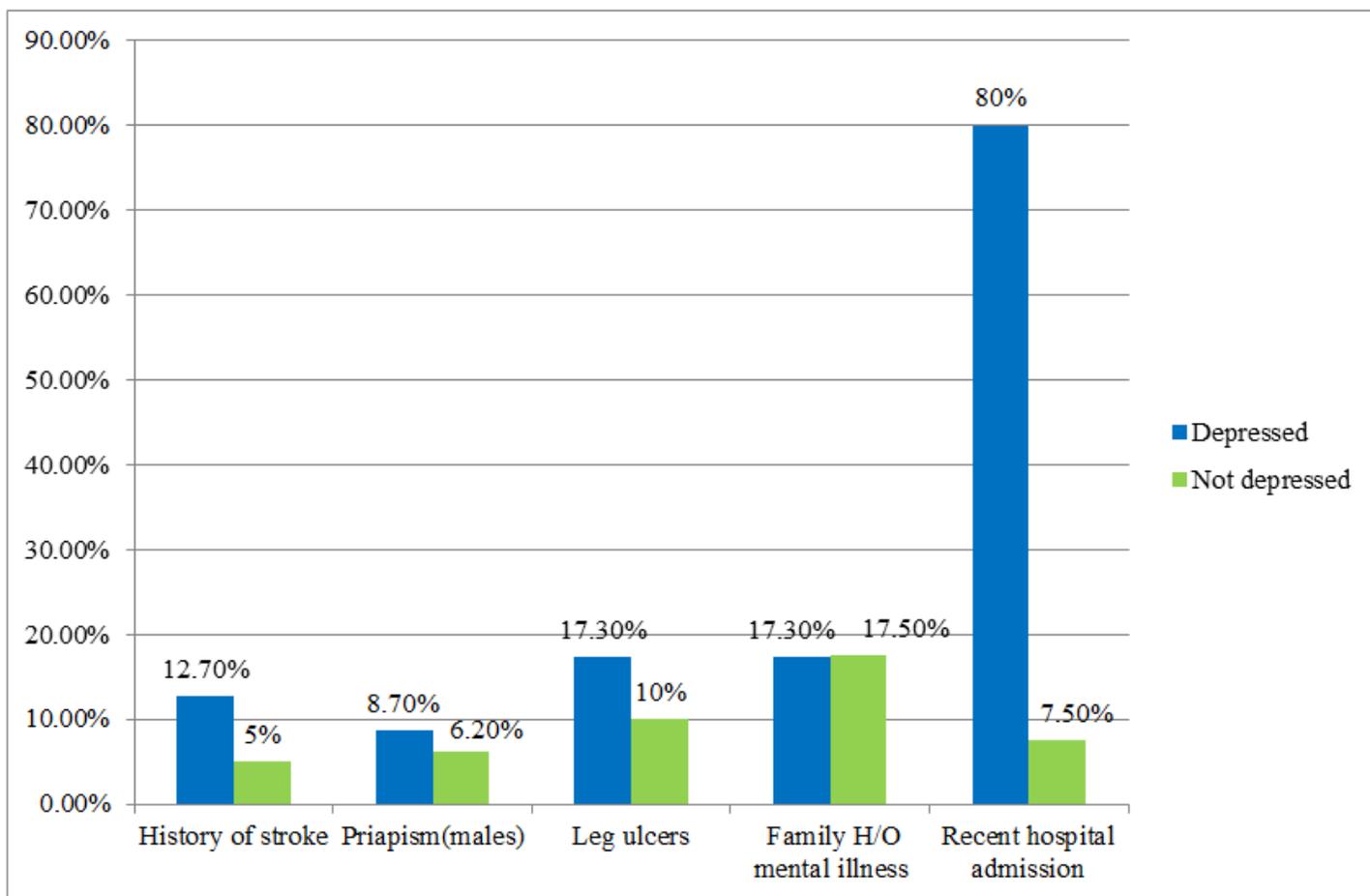


Figure 1

Distribution of clinical characteristics among the depressed and non-depressed study participants (N=255) in Mulago Kampala, February 2018