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Physical and psychiatric comorbidities among patients with severe mental illness as seen in Uganda

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Ethics approval and consent to participate The study obtained ethical approvals from the Uganda Virus Research Institute's Research and Ethics Committee (GC/127/19/10/612) and the Uganda National Council of Science and Technology (HS 2337). Participants were given information about the study by trained study Psychiatric Nurses/Psychiatric Clinical Officers and informed consent and assent sought before enrolment into the study. Participants found to have a SMI were provided healthcare and supported at the out-patient departments (OPDs) of their respective hospitals. Informed consent and assent were obtained from all the individual participants included in the study.

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Abstract

While psychiatric and physical comorbidities in severe mental illness (SMI) have been associated with increased mortality and poor clinical outcomes, problem has received little attention in low- and middle-income countries (LMICs). This study established the prevalence of psychiatric (schizophrenia, bipolar affective disorder, and recurrent major depressive disorder) and physical (HIV/AIDS, syphilis, hypertension and obesity) comorbidities and associated factors among 1201 out-patients with SMI (schizophrenia, depression and bipolar affective disorder) attending care at two hospitals in Uganda. Participants completed an assessment battery including structured, standardised and locally translated instruments. SMIs were established using the MINI International Neuropsychiatric Interview version 7.2. We used logistic regression to determine the association between physical and psychiatric comorbidities and potential risk factors. Bipolar affective disorder was the most prevalent (66.4%) psychiatric diagnoses followed by schizophrenia (26.6%) and recurrent major depressive disorder (7.0%). Prevalence of psychiatric comorbidity was 9.1%, while physical disorder comorbidity was 42.6%. Specific comorbid physical disorders were hypertension (27.1%), obesity (13.8%), HIV/AIDS (8.2%) and syphilis (4.8%). Potentially modifiable factors independently significantly associated with psychiatric and physical comorbidities were: use of alcohol for both syphilis and hypertension comorbidities; and use of a mood stabilisers and khat in comorbidity with obesity. Only psychiatric comorbidity was positively associated with the negative outcomes of suicidality and risky sexual behaviour. The healthcare models for psychiatric care in LMICs such as Uganda should be optimised to address the high burden of psychiatric and physical comorbidities.

Keywords

Physical and psychiatric comorbidities; Association; Potential risk factors; Healthcare models

Introduction

Mental illnesses are a major cause of morbidity and mortality globally, with low- and middle-income countries (LMIC) experiencing a rapid increase in rates of these disorders [1]; however, increase in these disorders is only partially justified due to the demographic changes (primarily by the growing number of mentally ill elderly persons and the increase in life expectancy) [2]; considerable increase in these disorders relates to the increased demand for psychiatric/psychological services influenced by the increased sensitisation/awareness and increasing diagnoses established by the increasing number of experts (psychiatrists, clinical psychologist, etc.) in mental health care [3, 4], plus increasing use of social media (online interaction which has taken precedence over face-to-face communication) that perpetuate isolation and loneliness [5]. Patients with severe mental illness (SMI) such as schizophrenia, depression and bipolar affective disorder die younger compared to the general population [6-8]. However, most of the increased mortality among people with SMI is attributed to comorbidity with other non-communicable diseases (NCDs) [6, 7, 9]. Patients with SMI experience a range of chronic physical health problems which may interfere with quality of life, increase health seeking behaviour and contribute to poor treatment outcomes

[10]. In turn, mental illness contributes to the NCD risks and outcomes through a number of mechanisms including adoption of harmful behaviours (such as sedentariness and smoking or excessive alcohol intake) which may affect treatment adherence and retention in care [1]. Second, some medications for SMI, particularly the second-generation antipsychotics are associated with increased risk of obesity, diabetes and metabolic syndrome [11]. Lastly, there is a tendency for comorbidity among patients with severe mental illnesses; there is an increased risk for the development of depression among patients with schizophrenia [12-14]; the overlap in the symptoms and genetic risk factors between psychiatric disorders suggests a common etiological mechanism [12].

Physical and psychiatric comorbidities have become increasingly important among people with SMI receiving care at mental health hospitals [15]. This is important because patients with comorbidity are generally happen to have higher rates of healthcare utilisation and poorer outcomes, in part because they are at risk of receiving suboptimal care for the co-existing conditions [16, 17]. However, comorbidity may provide an opportunity for patients to receive care beyond the index condition [18, 19]. This is best illustrated in HIV care in sub-Saharan Africa where the control of hypertension and other NCDs is better among HIV positive than HIV negative individuals, perhaps because individuals living with HIV have more regular and intensive contact with the healthcare system [20, 21].

Although comorbidity is of worldwide concern, the majority of evidence to date comes from high-income countries, with only a few studies from LMIC, and fewer from sub-Saharan Africa [1, 22]. These limited data suggest a high and increasing burden of comorbidity [22, 23], affecting relatively young people [24]. Although comorbidity is a global concern, which extends beyond LMIC to equally affect people in high-income countries [1], detection and management of mental and physical comorbidities will pose a particular challenge for LMIC healthcare systems, which historically have separated services for mental and physical health [1, 25]. Uganda experiences a high population growth rate (3.26) [26, 27], accommodates an increasing number of refugees and immigrants from other countries, has a population with genetic diversity and disease susceptibility across this diverse populations [28], making it suitable for comorbidity research. Since Uganda belongs to the LMICs whose healthcare system is challenged by mental and physical comorbidities, what is the prevalence of comorbidity, associated potential risk factors and negative outcomes among patients with severe mental illness (SMI) in rural (Masaka Regional Referral Hospital—Masaka district) and urban (Butabika National Referral Mental Hospital—Kampala capital city) in Uganda? Thus, the purpose of our study was to establish the prevalence of comorbidity, associated potential risk factors and negative outcomes among patients with severe mental illness (SMI) in rural (Masaka Regional Referral Hospital—Masaka district) and urban (Butabika National Referral Mental Hospital—Kampala capital city) Uganda.

Materials and methods

Study design and site

A cross-sectional study was undertaken among 1201 individuals with SMI attending care at the out-patient departments (OPDs) at Butabika National Referral Mental Hospital—Kampala capital city (central Uganda) and Masaka Regional Referral Hospital—Masaka

district (southwestern Uganda), enrolled between February and December 2018. To be eligible for the study, participants had to be adults over 18 years of age. Participants had to speak English or Luganda (the local language spoken in the study areas). Participants in need of immediate medical attention and those unable to understand the study's assessment instruments were excluded from the study.

Recruitment and data collection

Participants were randomly selected from over 3000 people recovering from mental illness and attending the out-patient departments (OPDs) at Butabika National Referral Mental Hospital—Kampala capital city (central Uganda) and Masaka Regional Referral Hospital—Masaka district (southwestern Uganda), enrolled between February and December 2018. On average, forty percent (40%) of the people with SMI attending OPDs at both Butabika National Referral Mental Hospital and Masaka Regional Referral Hospital were included in the study. Participants were given information about the study by trained Research Assistants (Psychiatric Clinical Officers and Psychiatric Nurses) and informed consent and assent sought before enrolment into the study. Research Assistants collected the data by administering questionnaire(s)/assessment battery [29-32]. Participants were not given incentives but they were given a transport refund (20,000/ = UShs). Participants found to have a SMI were provided healthcare and supported at the OPDs of their respective hospitals.

Measures

The assessment battery comprised of a structured and standardised, locally translated psychosocial instruments [29-32]. SMIs (schizophrenia, depression and bipolar affective disorder) were established using the MINI International Neuropsychiatric Interview version 7.2. Other standardised measures used in this study include: (a) the socio-economic index (SEI) which was constructed from commonly available household items in a typical Ugandan households, this has previously been used in Uganda by this study group [31, 33, 34]. The SEI was used as a measure of socio-economic status (SES). (b) The Multidimensional Scale of Perceived Social Support (MSPSS) was used to assess for social support [35]. The MSPSS is a 12-item instrument that was designed to assess perceptions about support from family, friends and significant others. The MSPSS has previously been translated into Luganda and used in local studies with good internal consistency ratios [30]. (c) The Stigma Scale was used to assess for mental health stigma [36]. This 28-tem questionnaire assesses for 'patient felt stigma' related to their mental illness. This instrument was used in the Ugandan socio-cultural context for the first time and it was therefore subjected to the translation process. (d) The Childhood Trauma Questionnaire-Short Form (CTQ-SF) assessed for adverse life events in childhood [37]. This is a 28-item questionnaire that asks about negative life events experienced as a child and as an adolescent. The CTQ-SF has previously been translated into Luganda and used in local studies with good internal consistency ratios[38]. (e) Items from the modified Adverse life events module of the European Parasuicide Interview Schedule (EPSIS) [29, 39] were used to assess for sexual abuse in adulthood. The items that were used to inquire about sexual abuse assessed for previous exposure to a given trauma in the two time periods, 'later in life (from onset of adulthood, 18 years to 12 months before the study)' and 'in the last 12 months'. Similarly,

the modified Adverse life events module of the European Parasuicide Interview Schedule (EPSIS) [29, 39] was used to assess for physical abuse in adulthood. The items that were used to inquire about physical abuse in adulthood assessed for previous exposure to a given trauma in the two time periods, 'later in life (from onset of adulthood, 18 years to 12 months before the study)' and 'in the last 12 months'. (f) The CAGE Substance Abuse Screening Tool [40] was used to assess for alcohol use and alcohol drinking problems. The name CAGE is an acronym formed by taking the first letter of key words (cut down, annoyed, guilty, eye opener) from each of the four screening questions. The CAGE questionnaire was developed in 1970 and remains one of the most reliable and easy screening instruments for the detection of alcoholism[40]. (g) HIV testing was undertaken using the HIV Determine strips for screening and the HIV Stat-pak for confirmatory test and SD Bioline as a tiebreaker based upon the algorithm recommended by the Uganda Ministry of Health [41]. (h) Syphilis testing was undertaken using Syphilis Antibody Rapid Test strips specific to Treponema pallidum as recommended by Uganda Ministry of Health [42]. The tools were administered by trained psychiatric nurse/psychiatric clinical officer research assistants who assessed among others the psychiatric diagnosis. The variables reported in this paper include: (i) socio-demographic factors (study site, gender, age category, religion, socio-economic status, and marital status), (ii) psychosocial factors (social support, mental health stigma, childhood physical abuse, childhood sexual abuse, physical abuse in adulthood and sexual abuse in adulthood), (iii) psychiatric illness factors (family history of psychiatric illness, past depressive episode, past manic episode, past psychotic episode, and life-time suicide attempt), (iv) psychotropic drugs (antiparkinsonian medication, mood stabilisers, 1st-generation neuroleptics, 2nd-generation neuroleptics, tri-cyclic antidepressants, and selective serotonin reuptake inhibitors) and (v) maladaptive behaviour (alcohol use, use of tobacco, alcohol drinking problem, use of marijuana, and use of khat) as laid out in the attached conceptual framework (Fig. 1). Details of all other measures and variables used in this study are attached; see Supplementary Table S7.

Statistical analysis

Statistical analyses were conducted using Stata release 15 (StataCorp, TX, USA). Socio-demographic characteristics were described using frequencies and percentages. A binary outcome variable "psychiatric comorbidity" was generated as having two or more of current/past depression or current/past mania or current/past psychotic episodes. The prevalence of psychiatric and physical disorders, psychiatric illness factors, maladaptive behaviour characteristics and morbidities were calculated at 95% CI.

To investigate the association between psychiatric and physical comorbidities with socio-demographic and psychosocial and psychiatric illness factors, a two-step procedure was adopted. During the first step, bivariate associations between each of the outcome variables (psychiatric/physical condition) and the independent variables was assessed using simple logistic regression models. In the second step, those socio-demographic, psychosocial and psychiatric illness factors that attained a level of significance of $P \leq 0.1$ (liberal cutoff point) at bivariate analyses were included in the final multivariate logistic regression model that assessed for the factors that were independently significantly associated with psychiatric and physical comorbidities.

The association between the physical and psychiatric comorbidities with negative behavioural and clinical outcomes was investigated by fitting logistic regression models for binary outcomes and ordinal logistic regression models for ordinal outcomes adjusted for study site, age and gender.

Results

Characteristics of study participants

Out of the 1201 participants enrolled into this study, 39.7% were between 35 and 49 years and 32.1% were between 25 and 34 years; mean age (with standard deviation) was 37.6 (11.7). The urban and rural study sites contributed 58% and 42% of participants, respectively. About a third of the participants were single (38.7%) or married (32.0%) and a quarter (24.6%) separated/divorced, with 4.7% widowed. Males and females enrolled in the study were 46% and 54%, respectively. Christians were 81% and Muslims were 18%. More than half (57.2%) of the respondents had at least 7 years of formal education. A third (32.9%) had suffered childhood physical abuse and a quarter (24.7%) childhood sexual abuse. Physical abuse in adulthood was reported by 34.1%, while sexual abuse in adulthood was reported by 21.9%. About two-thirds (61.0%) reported a family history of psychiatric disorder (see Table 1).

Pattern of psychiatric and physical comorbidities

Bipolar affective disorder was the most prevalent (66.4%) primary psychiatric diagnoses followed by schizophrenia (26.6%) and recurrent major depressive disorder (7.0%). Psychosis was the most prevalent (22.2%) current psychiatric episode followed by depressive episode (13.5%) and manic episode (6.2%). Psychiatric comorbidity was reported by 9.1% of respondents, while physical disorders/problems' comorbidities were reported by 42.6%. The specific comorbid physical disorders/problems were 27.1% hypertension, 13.8% obesity, 8.2% HIV/AIDS and 4.8% syphilis (see Table 2).

Socio-demographic factors associated with psychiatric and physical comorbidities at bivariate analysis

Table 3 shows the association between psychiatric and physical comorbidities with socio-demographic factors at bivariate analyses. On psychiatric comorbidity, while increasing age was associated with increased odds of having an additional psychiatric disorder, rural residence was associated with reduced odds of having an additional psychiatric disorder compared to urban residence. On HIV, the following factors were associated with increased odds of being HIV positive: female gender, increasing age, widowed compared to being married, on the other hand, being Moslem was associated with reduced odds of being HIV positive compared to being Christian. On syphilis, the following factors were associated with increased odds of having syphilis: increasing age, and widowed compared to being married; on the other hand, increasing socio-economic index was associated with reduced odds of having syphilis. On hypertension, the following factors were associated with increased odds of having hypertension: increasing age, and widowed compared to being married, on the other hand, rural residence was associated with reduced odds of having hypertension compared to urban residence. On obesity, the following factors were associated

with increased odds of being obese: female gender, increasing age, and increasing socio-economic index; on the other hand, rural residence was associated with reduced odds of being obese compared to urban residence. Those variables that met the liberal cutoff point of $P \leq 0.1$ were then included in the final multivariate model.

Psychosocial and psychiatric illness factors associated with psychiatric and physical comorbidities at bivariate analysis

Supplementary Table S4 shows the association between psychiatric and physical comorbidities and psychosocial and psychiatric illness factors at bivariate analyses. On psychiatric comorbidity, the following factors were associated with increased odds of having an additional psychiatric disorder: increasing mental health stigma, childhood physical abuse, physical abuse in adulthood, sexual abuse in adulthood, use of antiparkinsonian drugs, and use of mood stabilisers; on the other hand, increasing social support and use of tri-cyclic anti-depressants was associated with reduced odds of having an additional psychiatric disorder. On HIV, the following factors were associated with increased odds of being HIV positive: childhood sexual abuse and sexual abuse in adulthood, on the other hand, a history of a past psychotic episode was associated with reduced odds of being HIV positive. For both syphilis and hypertension, only alcohol use was associated with increased odds of having either syphilis or hypertension. On obesity, the following factors were associated with increased odds of being obese: sexual abuse in adulthood, past depressive episode and use of mood stabilisers.

Final multivariate model of socio-demographic, psychosocial and psychiatric illness factors associated with psychiatric and physical comorbidities

Supplementary Table S5 shows the factors that were independently significantly associated with each of the investigated comorbidities after fitting the final multivariate model. For psychiatric comorbidity, only increasing age was independently significantly associated with increased odds of having a comorbidity. For HIV, female gender, being a Moslem (compared to being a Christian) and having a suffered a past psychotic episode, were independently significantly associated with increased odds of having a comorbidity. For syphilis, only being widowed (compared to being married) was independently significantly associated with increased odds of having a comorbidity. For hypertension, rural residence (compared with urban residence), increasing age and use of alcohol were independently significantly associated with increased odds of having a comorbidity. For obesity, rural residence (compared to urban residence), female gender, increasing age, increasing socio-economic index, use of a mood stabiliser and use of khat were independently significantly associated with increased odds of having a comorbidity.

Association between negative behavioural and clinical outcomes and psychiatric and physical comorbidities

Only psychiatric comorbidity was positively associated with the negative outcomes of life-time attempted suicide and risky sexual behaviour. None of the other investigated comorbidities were associated with the investigated negative behavioural and clinical outcomes (see Table 4).

Discussion

This study demonstrates a high prevalence of physical and psychiatric comorbidities, associated potential risk factors and negative outcomes among patients with severe mental illness (SMI) attending out-patients' departments (OPD) at Butabika and Masaka hospitals in Uganda. According to this study, comorbidity between psychiatric disorders and physical disorders was reported by 13.1% of the respondents, a figure that was a third of that reported in a meta-analysis done on papers mostly from western countries where a pooled prevalence was 36.6% [43]. Obviously, difference between prevalence rates established by this study (cross-sectional at baseline) and the meta-analysis by Daré et al. [43] relate to the different study designs. Similarly, the prevalence of psychiatric disorders in people with chronic physical diseases living in developing and emerging countries is comparable to those in developed countries [43]. Importantly, the relationship between medical and psychiatric illness involves multiple factors [44], and happens to be bi-directional; physical illness can cause the mental illness but also the mental illness can cause the physical illness [45]. The co-occurrence of psychiatric and physical disorders is supported by the mind–body interaction (substance dualism) suggested by Descartes (1641) as described by Nadler and Morris [46].

The prevalence of psychiatric comorbidity (presence of at least two current psychiatric disorder episodes) reported in this study was 9.1%, which was much lower than the 24% of respondents who met the criteria for two psychiatric disorders in a study about the prevalence of psychiatric disorders on the general wards of Mbarara regional referral hospital in Southwestern Uganda; both studies used the Mini International Neuropsychiatric Interview (MINI) to determine specific psychiatric diagnoses but this study interviewed participants attending out-patient departments (OPDs), while the study by Rukundo et al. [44] interviewed admitted patients. Arguably, the lower prevalence of psychiatric comorbidity reported in this study compared to the prevalence rates reported by other studies relates to the environment under which the study was conducted, level of education/training of interviewers (Research Assistants who interviewed participants in this study were trained Psychiatric Nurses and Psychiatric Clinical Officers who used a more strict criteria to gather information), quality of data, the culture of the study population, participants' access to psychiatric services and the level of development of psychiatric services. The degree of psychiatric morbidity happens to be directly related to indicators of family adversity, physical abuse, other psychosocial variables [47], and interpersonal adversity experienced since childhood [48]. Similarly, poverty, homelessness, substance use, and smoking all augment the risk of both physical and psychiatric illnesses [45].

Psychiatric comorbidities are so common and might be integral to schizophrenia [49]. Commonly, the symptomatology of schizophrenia over-shadows other psychiatric disorders; thus, it is difficult to determine primacy but the alternative approach adopted by Diagnostic and Statistical Manual of Mental Disorders (DSM-IV R) was to consider these symptoms as part of another axis I diagnosis that occurs alongside schizophrenia [50]; however, the current DSM-5 moved to a non-axial documentation of diagnosis (melding of Axes I, II, and III) to reflect the view that different mental disorders are fundamentally conceptualised in a similar way, integrating biological, physical, behavioural, and psychosocial factors

and processes [51]. Possibly, depressive symptoms in schizophrenia are associated with antipsychotic medications that produce neurological side effects like Parkinsonism (particularly bradykinesia, diminution of affective expression, masked facies, and verbal delays) and akathitic restlessness that may be confused with the psychomotor retardation or agitation of depression [49]. Antipsychotic drugs may also produce a primary dysphoria, possibly due to dopamine blockade in reward pathways, and it has even been suggested that these drugs are innately depressogenic [49]. Similarly, the classic construct of depression in schizophrenia is that of post-psychotic depression (PPD), defined in an appendix of the DSM-IV R [50], as a major depressive episode that is superimposed on, and occurs only during the residual phase of schizophrenia; however, the current DSM-5 ruled out depressive or bipolar disorder with psychotic features [51]. Traditionally, depression in schizophrenia has been formulated as a psychological reaction to loss or to the psychological trauma of the psychotic episode [49]. Arguably, depression is a reaction to psychosis, or represents an unmasking effect of the depression as the psychosis remits [49]. Similarly, there is a clear substantial comorbidity index between bipolar disorder and schizophrenia [52, 53].

On the individual physical comorbidities, this study reported a rate for HIV comorbidity of 8.2% in contrast with the national general population prevalence of HIV of 5.7% [54]. Two earlier Ugandan studies reported higher rates of HIV comorbidity among patients with SMI, a rate of 18.4% in 2011 [55] and a rate of 11.3% in 2013 [56], which contrasted with the national general population prevalence of HIV of 7.3% [57, 58]. In all these three studies, the rate of HIV among patients with SMI was generally higher than that in the general population, suggesting that patients with SMI have increased vulnerability to HIV compared to the general population. In this study, syphilis comorbidity was reported at a rate of 4.8%, in contrast with the Uganda national prevalence rate of 2.9% in 2016 among women attending antenatal care [59]. Both vulnerability to HIV and syphilis which are predominantly transmitted through heterosexual relationships in the SMI context in Uganda are underlined by a common vulnerability to risky sexual behaviour and sex violence which Lundberg and colleagues (2015) in their Ugandan study reported to be more prevalent among people with SMI than in the general population [60].

According to this study, the most prevalent physical comorbidity was hypertension (27.1%), which contrasted with the Ugandan general population rate of hypertension of 26.4% [61]. This rate of comorbid hypertension in SMI established by this study is much higher than that reported by two earlier UK studies, a rate of 19% in 2014 [62] and a rate of 18.3% in 2015 [63], in contrast to the general population rate of hypertension in the UK of 26.2% in 2017 [64].

The prevalence of comorbid obesity established by this study (13.4%) contrasted with the Ugandan general population rate of obesity of 7% [65]. A study among patients with SMI in the USA (published in 2010) reported a rate of obesity of 52% [66], in contrast with the general population rate of 35.7% in 2009–2010 [67]. Factors underlying the association between SMI and the cardiovascular risk factors of hypertension and obesity in the USA include a variety of lifestyle factors such as smoking, lack of physical activity, and poor diet [66].

The presence of psychiatric disorders in medically ill patients increases the cost of health care due to repeated ineffective use of services, increased length of hospital stay, hospitalisation rates and mortality [44]. It is for this reason that the World Health Organization recommended the integration of mental health services into general health care services [68], to effectively and efficiently respond to the psychiatric and physical comorbidities [43].

Pattern of psychiatric and physical comorbidities among patients with severe mental illness in Uganda

The clustering of psychiatric disorders (with participants having two or more current psychiatric disorders) relates to the previous literature which suggests that chronic physical, infectious and mental health conditions commonly co-exist [1, 69]. A previous study established that psychiatric conditions (such as schizophrenia, depression, and bipolar affective disorders) cluster with a range of physical NCDs as well as with chronic infections such as HIV [16]. In addition to ageing, increased prevalence of comorbidity among people in low- and middle-income countries (LMICs) relates to a growing prevalence of NCDs (such as an increase in obesity and physical inactivity) in addition to the well-known burden of infectious diseases like HIV/AIDS [69]. This change in condition patterns reveals the changing lifestyle, cultural behaviours, changing environmental exposures, urbanisation, and healthcare-related advances that contribute to an increased prevalence of chronic conditions [70, 71]. The relationship between mental health and physical conditions appears to be bi-directional and may arise due to shared biological factors, or mediated by various lifestyle and treatment specific factors [16]. Similarly, the clustering of physical comorbidity with index psychiatric disorders was high because comorbidity is generally higher among mentally sick people who happen to be more vulnerable, socioeconomically disadvantaged, often have a lower capacity to access healthcare and deal with the burden of ill health [69, 72]. Relatedly, some studies have found that those with comorbidity (especially those on antipsychotic treatment) are at particular risk of adverse drug events [73] and are at risk of receiving suboptimal care for co-existing physical conditions [16, 17]. Conditions appear to cluster in many LMICs in which HIV infection is common and the use of ART widespread [70]. It has been established that use of antiretroviral therapies (ART) for the treatment of HIV has been associated with insulin resistance, elevated blood lipids, and central fat accumulation, each of which can ultimately contribute to the development of type 2 diabetes and cardiovascular diseases [69]. Depression has also been shown to increase the risk of morbidity and mortality in populations with type 2 diabetes [74]. Some psychotropic medications, most notably antipsychotics, have also been reported to be associated with increased risk of several physical conditions including obesity, diabetes, cardiovascular diseases, and haematological diseases [75, 76]. It has also been suggested that chronic inflammation and oxidative stress may underlie a number of other chronic conditions and cancers, and could therefore also contribute to several comorbidity clusters [77-80]. Given the common co-occurrence of mental and physical health conditions in the context of comorbidity, there is a need for better evidence about causality and confounding to identify the exacerbatory effects of medications on those with comorbidity.

Factors associated with comorbid psychiatric and physical disorders

The potentially modifiable factors that were independently significantly associated with psychiatric and physical comorbidities in this study were: use of alcohol in both syphilis and hypertension comorbidity, use of a mood stabilisers and khat in comorbidity with obesity. While a number of potentially modifiable psychosocial factors including social support, mental health stigma, exposure to childhood and adulthood physical and sexual abuse were associated with psychiatric comorbidity at bivariate analyses, these associations were not independently significantly associated with psychiatric comorbidity at multivariate analyses. These findings suggest that these psychosocial factors individually may be making only a small contribution to the overall risk for psychiatric comorbidity. Indeed, Cerdá et al., 2009 in a systematic review have reported varied contribution to risk for psychiatric comorbidity by environmental and genetic factors depending on the combination of psychiatric disorders making up the comorbidity [81]. In this study, we did not explore the factors associated with the different psychiatric comorbidity combinations due to the limited sample size of the different psychiatric comorbidity sub-types.

In this study, alcohol use was positively associated with syphilis comorbidity, a finding that has previously been reported by other authors, who found a high correlation between alcohol use and sexually transmitted diseases (STDs) because alcohol use strongly influences men and women to engage in risky activities [82, 83]. Alcohol use in this study was also positively associated with hypertension comorbidity; a finding that has previously been reported and attributed to changes in biochemical pathways [84, 85]. In this study, mood stabilisers were positively associated with obesity, this finding has previously been reported where mood stabilisers were associated with an increased risk for several physical diseases, including obesity, dyslipidemia, diabetes mellitus, thyroid disorders, hyponatremia; cardiovascular, respiratory tract, gastrointestinal, haematological, musculoskeletal and renal diseases, as well as movement and seizure disorders [76]. Use of khat was positively associated with obesity comorbidity; evidence from a recent review of studies suggests that different khat extracts or cathinone produces changes in lipid metabolism that may explain this observation [86].

Negative behavioural and clinical outcomes associated with comorbid psychiatric and physical disorders

In this study, psychiatric comorbidity was positively associated with the negative outcome of life-time attempted suicide. Findings from this study are in agreement with a previous study which demonstrated that suicide risk is elevated among people with both physical and psychiatric illnesses (comorbidity) due to the double burden of both conditions [87]. Similarly, psychiatric comorbidity was positively associated with risky sexual behaviour. Findings from this study are in agreement with a previous study which suggested an association between risky sexual behaviour and psychiatric disorders possibly as a symptom of the disorder (bipolar disorder) and/or due to loss of insight [88].

This study has many strong points such as the use of an adequate sample size of 1,201 respondents, use of standardised assessment instruments to diagnose psychiatric disorders and for the assessment of psychosocial constructs such as social support. However, the

study had some limitations to consider when interpreting the findings. First, this being a cross-sectional study, it was not possible to determine the direction of causality between the independent and dependent factors. Second, the study only considered a few psychiatric diagnoses (schizophrenia, bipolar affective disorder and recurrent major depressive disorder) and physical (HIV/AIDS, syphilis, hypertension and obesity) comorbidities due to limitations of resources. Thirdly, in investigating the associations of comorbidity, due to having multiple variables and hence the need to have multiple testing, there was a risk of both confounding and having false positive associations. To minimise these risks at analyses, we undertook a robust two-step analyses procedure that involved an initial bivariate logistic regression step with a liberal cutoff point of $P \leq 0.1$ for selecting variables that were taken into the second step multivariate model. Despite these limitations, to the best of our knowledge, this is the first study to establish the prevalence of physical and psychiatric comorbidities and associated risk factors among patients with severe mental illness attending Butabika National Psychiatric Referral Hospital and Masaka Regional Referral Hospital.

Suggestions/recommendations

While these study findings point to a considerable burden of psychiatric and physical comorbidities among patients with severe mental illnesses in the sub-Saharan African setting of Uganda, psychiatric services in Uganda currently pay little attention to the possible co-occurrence of physical disorders. As a recommendation, there is need to integrate the screening and management of physical disorders within psychiatric services. The prominence of alcohol use as a potential risk factor in both syphilis and hypertension comorbidity calls for highlighting this risk in health education messaging for patients with severe mental illness.

Conclusion

Based upon the findings in this study, there is considerable psychiatric and physical comorbidities among patients with severe mental illness in Uganda. To address this burden, there is need to integrate physical health services into psychiatric health care. Another observation of this study is that the potentially modifiable factors of use of alcohol and the use of the recreational substance of khat could be targeted by public health interventions in addressing the problem of physical comorbidity in severe mental illness. This study has also highlighted the fact that psychiatric comorbidity may be a risk factor for both suicidality and risky sexual behaviour in severe mental illness.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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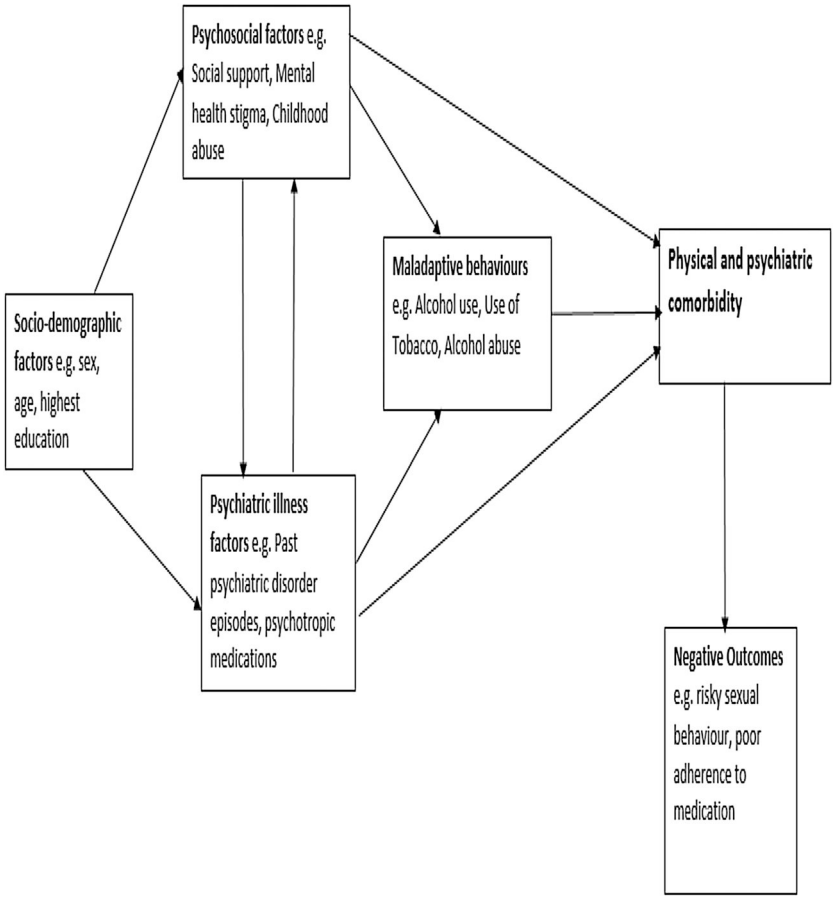

Fig. 1.
Conceptual framework on comorbidity in severe mental illness

Table 1:

Socio demographic and psychosocial characteristics

Factor	Frequency(n = 1201)	(%)
Site		
Butabika(urban)	701	58.4%
Masaka(rural)	500	41.6%
Gender		
Male	547	45.5%
Female	654	54.5%
Age		
Mean(SD)	37.6(11.7)	
Age		
<25	138	11.5%
25 – 34	384	32.1%
35 – 49	475	39.7%
>=50	200	16.7%
Socio-economic status(grouped)		
0 – 2	189	15.7%
3 – 4	409	34.1%
5 – 6	486	40.5%
7 - 8	117	9.7%
Marital status		
Currently married	384	32.0%
Widowed	57	4.7%
Separated/divorced	295	24.6%
Single	464	38.7%
Employment status		
Farmer/fisherman	304	25.4%
Professional	139	11.6%
Informal employment	206	17.2%
Unemployed	549	45.8%
Religion		
Christian	977	81.3%
Moslem	212	17.6%
Others	10	0.83%
Education level		
No formal education	37	3.1%
Primary	476	39.6%
Secondary	460	38.3%
Tertiary	227	18.9%
Psychosocial factors		
Childhood physical abuse	395	32.9%

Factor	Frequency(n = 1201)	(%)
Childhood sexual abuse	296	24.7%
Physical abuse in adulthood	409	34.1%
Sexual abuse in adulthood	263	21.9%
Family history of psychiatric illness	731	61.0%

Socio economic status assessed using eight (8) household items owned

Table 2:

Pattern of psychiatric and physical comorbidities among respondents

Factor	N=1201	Prevalence (95% CI)
Primary psychiatric diagnoses		
Schizophrenia	320	26.6%
Bipolar affective disorder	797	66.4%
Recurrent major depressive disorder	84	7.0%
Comorbid physical disorder/problem		
HIV/AIDS	87/1057	8.2% (6.7% - 10.0%)
Syphilis	53/1095	4.8% (3.7% - 6.3%)
Hypertension	326/1201	27.1% (24.7% - 29.7%)
Obesity	165/1193	13.8% (11.9% - 15.9%)
Had at least one comorbid physical disorder/problem	512/1201	42.6 %(39.8% - 45.4%)
Had at least two comorbid physical disorder/problem	109/1201	9.1 %(7.5% - 10.8%)
Current psychiatric episode & comorbidity		
Manic episode	74/1196	6.2 %(4.8% - 7.6%)
Psychotic episode	263/1187	22.2 %(20.0%- 24.8%)
Depressive episode	160/1189	13.5 %(11.5% - 15.4%)
Did not meet criteria for at least one current psychiatric disorder episode	831/1201	69.1 %(66.5% - 71.7%)
At least one physical and one psychiatric comorbidity	157/1201	13.1 %(11.3% - 15.1%)
Had at least two current psychiatric disorder episodes	109/1201	9.1 %(7.5% - 10.8%)

Hypertension ;Sys>=140 dia>=90

BMI>=30; obesity

Table 3:

Socio-demographic factors associated with comorbid psychiatric and physical disorders at bivariate analysis

Factor	PSYCHIATRIC COMORBIDITY*	HIV*	SYPHILIS*	HYPERTENSION*	OBESITY*
Study site					
Butabika	1	1	1	1	1
Masaka	0.51(0.39;0.67)	1.09(0.70;1.69)	0.76(0.43;1.35)	0.66(0.50;0.86)	0.45(0.31;0.65)
	P<0.001	P=0.712	P=0.353	**P=0.002**	**P<0.001**
Sex					
Male	1	1	1	1	1
Female	1.22(0.93;1.59)	2.67(1.61;4.43)	1.28(0.73;2.25)	1.00(0.77;1.29)	4.66(3.07;7.09)
	P=0.154	**P<0.001**	P=0.393	P=0.987	**P<0.001**
Age category					
18 – 24	1	1	1	1	1
25 – 34	1.36(0.88;2.10)	1.62(0.60;4.39)	1.73(0.49;6.12)	1.33(0.78;2.26)	3.61(1.41;9.30)
35 – 49	1.81(1.18;2.78)	2.66(1.03;6.88)	1.75(0.51;6.08)	2.57(1.56;4.25)	5.57(2.21;14.02)
>=50	1.27(0.78;2.06)	2.58(0.93;7.20)	4.84(1.40;16.71)	3.71(2.16;6.40)	5.06(1.92;13.34)
	P=0.038	**P=0.083**	**P=0.003**	**P<0.001**	**P=0.001**
Religion					
Christian	1	1	1	1	1
Moslem	1.16(0.81;1.67)	0.32(0.14;0.75)	0.94(0.45;1.95)	0.77(0.54;1.09)	1.00(0.65;1.55)
	P=0.703	**P=0.009**	P=0.861	P=0.338	P=0.975
SES index					
Per unit increase	1.03(0.96;1.11)	0.86(0.76;0.97)	0.97(0.83;1.13)	1.05(0.98;1.13)	1.18(1.07;1.30)
	P=0.424	**P=0.017**	P=0.686	P=0.189	**P=0.001**
Marital status					
Married	1	1	1	1	1
Widowed	1.17(0.58;2.36)	3.49(1.60;7.61)	4.41(1.83;10.65)	2.17(1.23;3.83)	1.75(0.90;3.39)
Separated	1.05(0.73;1.52)	1.39(0.79;2.44)	1.56(0.76;3.17)	1.05(0.75;1.47)	1.00(0.66;1.53)
Single	0.83(0.60;1.14)	0.72(0.40;1.29)	0.66(0.31;1.43)	0.78(0.57;1.06)	0.58(0.38;0.88)
	P=0.450	**P=0.001**	**P<0.001**	**P=0.003**	**P=0.004**

* **Note:** Unadjusted Odds; **Bold** indicates variables that met the liberal cut-off point of P ≤0.1 for inclusion in final multivariate model ; SES – Social Economic Status

Table 4

Negative behavioural and clinical outcomes associated with comorbid psychiatric and physical disorders

Factor	Psychiatric comorbidity*	HIV*	Syphilis*	Hypertension*	Obesity*
Behavioural outcomes					
Lifetime suicide attempt—yes	1.99 (1.44; 2.74)	1.05 (0.61; 1.82)	0.94 (0.46; 1.92)	0.76 (0.55; 1.07)	1.26 (0.83; 1.91)
	***P* < 0.001**	*P* = 0.857	*P* = 0.878	*P* = 0.121	*P* = 0.271
Risky sexual behaviour—yes	1.77 (1.28; 2.30)	1.46 (0.88; 2.40)	1.44 (0.77; 2.70)	0.89 (0.65; 1.22)	0.75 (0.49; 1.15)
	***P* < 0.001**	*P* = 0.140	*P* = 0.250	*P* = 0.469	*P* = 0.186
Clinical outcomes					
Missed taking psychiatric medications—yes	1.01 (0.75; 1.36)	0.81 (0.46; 1.43)	0.85 (0.41; 1.73)	0.79 (0.57; 1.09)	0.78 (0.51; 1.21)
	P = 0.945	*P* = 0.460	*P* = 0.649	*P* = 0.156	*P* = 0.271
Missed taking oral ART—yes	1.61 (0.28; 9.13)	0.13 (0.01; 2.35)	3.86 (0.49; 30.3)	1.49 (0.22; 10.02)	–
	P = 0.589	*P* = 0.169	*P* = 0.199	*P* = 0.684	

ART antiretroviral therapy

*Adjusted for study site, sex and age; bold indicates associations that were significant at $P \leq 0.05$