

Clinical Predictors of Duration of Untreated Psychosis: Exploring Psychosocial and Clinical Predictors of Duration of Untreated Psychosis in First-Episode Psychotic Patients in Mzuzu, Malawi

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Abstract

Introduction

The duration of untreated Psychosis (DUP) is a modifiable factor in the management and outcome of patients with psychosis. However, its predictive factors have not been studied much in Malawi. Our study was aimed at determining the psychosocial and clinical predictors of DUP in first episode psychosis in Malawi.

Method

A quantitative cross-sectional study, using secondary data from an early intervention study project was done in Mzuzu, Malawi. We analysed 140 adult participants enrolled in early intervention project in 2010. Data was collected using abstraction sheet to target predictive factors. We conducted univariate and multivariate logistic regression at confidence interval of 95%. We described the mean DUP, and looked at relationship of clinical and psychosocial factors with DUP.

Results

Most participants were male (60%, n=84) and single (51.4%, n=72). The median age of male participants was 31 years (Range=18 to 60), lower than females 35 years (Range=18 to 65). (what were the numbers of females). The majority of the participants' highest education level was secondary school (63.6%, n=89), and most had DUP of ≥ 6 months (74%, n=103). We found mean DUP of 42 months (SD= ± 71). Employment status, diagnosis of schizophrenia (OR=10.93, 95% C.I 3.08-38.89), and negative symptoms of psychosis were associated with DUP of ≥ 6 months. Public self-consciousness and social quality of life were associated with long DUP.

Conclusion

Our study shows psychosocial and clinical factors that predict long DUP in Malawi. This highlights the need to target these factors when working on first episode psychosis for a better outcome.

Key words: Duration of untreated psychosis, First episode psychosis, psychosocial factors, Clinical factors

Introduction

Psychosis is one of the disabling conditions in a group of mental, neurological and substance use disorders (MNS). MNS accounts for 10.4 % of the Disability-Adjusted Life Years (DALYs) globally^{1,2}. Progression of psychosis such as Schizophrenia, tends to be slow and can sometimes take time to be noticed by client or carers³. Psychosis contributes substantially to mental health burden and societal expenditure on global level⁴. Treatment delay of MNS has been reported in both low- and middle-income countries (LMICs), and in high income countries (HICs)¹. This tends to lengthen duration of untreated psychosis (DUP)⁵.

Duration of Untreated Psychosis (DUP) is time from the appearance of first psychotic symptoms to initiation of adequate antipsychotic treatment⁶. Studies have indicated the effect of DUP on the brain structures and eventually having an effect on the proper functioning of the brain⁷. Malla et al, reports that DUP is associated with orbital-frontal grey matter volume reduction⁷. This explanation supports a possible neurotoxic effect of prolonged untreated psychosis⁸. DUP is argued to be an important concept

and a modifiable factor in management and outcome of patients with psychosis⁹. Addington et al, observed that DUP is one of the important prognostic factors because it can be minimized by promoting early detection and proper treatment referrals⁹. Long DUP has been associated with poor treatment response and overall poor social functional outcome of people with psychosis¹⁰. Given this explanation, it is important to understand the factors that predict DUP in first episode psychosis to reduce effects of prolonged DUP.

DUP has been categorized as long and short using a cut off of 6 months i.e., participants with DUP of greater than 6 months are considered to have long DUP¹¹. Given the explained cut off of DUP, Addington et al, reports a long DUP which is associated with the young age of onset of psychotic symptoms⁹. In adult studies of participants with psychosis, DUP of 17 months, 16 months, 35 months have been reported in China, Singapore, and Japan respectively^{10,11}. The following clinical and psychosocial correlates were found to be associated with DUP: slow mode of onset of psychosis, hospitalisation, a diagnosis of schizophrenia, poor insight and younger age at onset of the disorder^{10,11}.

However, in Malawi, there are less early intervention

Study population

We used first episode psychosis patients who were enrolled in the parent study that examined the duration of untreated psychosis in 2011 at Saint John of God Mental Hospital, Malawi. First episode psychosis patients in our study referred to all patients that had a diagnosis of psychosis for the first time and had never been on effective treatment for the disorder.

Sample size and sampling technique

The sample size was calculated using an estimation in a single proportion which is given by the formula: . Using the reported global treatment gap of 90% for MNS in developing countries¹ as expected prevalence (p), margin error (E) of 5%, and 1.96 as Z value corresponding to 0.05 significant level; the sample size of 138 was adequate for our study. However, the parent study recruited 140 participants, we therefore analysed all 140 recruited participants for our study.

Ethical considerations

Our study got approval from College of Medicine Research Ethics Committee (COMREC) in September, 2017, (certificate number P.09/17/2262). Permission to use the secondary data for the study at the mentioned site was granted by the Executive Director of Saint John of God Hospital Services, Malawi. To ensure privacy and confidentiality, codes were used on the participants name in the abstraction sheet.

Data collection

We abstracted data using an abstraction sheet. The variables which were abstracted from the parent study access database were: social demographic characteristics such as sex, age, marital status, education level and employment status. Clinical variables included mental disorder diagnosis, positive symptoms of psychosis, negative symptoms of psychosis, insight of patients to the illness, patients’ attitude towards drugs, depressive symptoms and level of functioning. Other Psychosocial factors included were

multi-dimensional health locus of control (MHLC) measured using MHLC scale¹⁹, quality of life measured using WHO quality of life scale²⁰, and the inner and self-feeling measured using self-consciousness scale²¹. All these tools are validated¹⁹⁻²² outside Malawi in similar group of participants. Tools were adopted to be used in Malawi and data collectors were trained in the use of the tools in the parent study. Similarly, a diagnosis of mental disorder was made using Structured Clinical Interview for Diagnostic and Statistical Manual for Mental disorders version-IV (SCID I)²³. SCID 1 is a structured diagnostic interview tool that was adapted for use in Malawi in psychiatric research studies, including cross-national epidemiological and treatment studies¹¹. It has also been validated

programs for first episode psychosis as compared to HICs¹². Chiliza et al, reports that in LMICs, DUP is longer and also associated with poor outcome¹⁵. DUP of 37 months in adult’s population, and DUP of 7 months among adolescents in Egypt and South Africa respectively has been reported^{14,15}. The reported DUP in other LMICs countries is not different with what was found in a Malawi study which reported DUP of 52 months¹⁶. However, it is important to understand the factors that predict DUP in our setting in order to intervene to reduce DUP.

Studies in Malawi have not explored most of the factors that predict DUP. An understanding of predictors of DUP will help inform strategies aimed at reducing DUP such as psycho education messages to the public on early symptoms identification of psychosis and prompt treatment^{17,18}. Knowledge of DUP predictors also informs mental health workers and other experts in the field on the factors to consider when planning for an early intervention service. Prompt treatment initiation gets enhanced given the knowledge on what to target in order to reduce DUP, hence secondarily preventing the disabilities that comes with the disorder if it is untreated for a longer period¹⁸. Proper referral procedures and treatment are also enhanced by general health practitioners. The current study therefore uses secondary data to explore psychosocial and clinical factors that predict long DUP in first episode psychosis in Malawi.

Methodology

Study design and setting

We conducted a cross –sectional, descriptive quantitative study using secondary data from an early intervention study project in Mzuzu, Malawi. We conducted the study at Saint John of God Mental Hospital in Mzuzu, Malawi. The secondary data that we used was collected from district Hospital catchment areas of Mzimba, Rumphu and Mzuzu town, Malawi.

Table 1: Socio demographic characteristics of study participants by Gender

Variable	Total sample: N=140 n(%)	Male N=84 n(%)	Female N=56 n(%)	P value
Age (median, range)	33(47)	31.0 (42.0)	35.0 (47.0)	0.17
Marital Status, n (%)				0.53
Married	68 (48.6)	39 (57.4)	29 (42.7)	
Single	72 (51.4)	45 (62.5)	27 (37.2)	
Employment				0.17
Unemployed	75 (53.6)	49 (65.3)	26 (34.7)	
Employed	65 (46.4)	35 (53.9)	30 (46.2)	
Education level				0.83
Primary	51 (36.4)	30 (58.8)	21 (41.2)	
Secondary	89 (63.6)	54 (60.7)	35 (39.3)	
Diagnosis				0.13
Schizophrenia	93 (66.4)	60(64.5)	33 (35.5)	
Schizoaffective	47 (33.6)	24 (51.1)	23 (48.9)	

Table 2: Logistic regression for DUP and Psychosocial and Clinical factors

Risk factor	DUP		Unadjusted OR (95% CI)	Adjusted OR (95% CI)
	<6 months n(%)	≥ 6 months n (%)		
	(n=37,26%,)	(n=103, 74%)		
Gender: Male	22 (26.2)	62 (73.8)	0.97 (0.45-2.09)	
Age (median, range)	29 (47)	34 (47)	1.03(1.00-1.07)*	0.97(0.91-1.02)
Marital status: Married	21 (30.9)	47(69.1)	1.56 (0.73-3.33)	2.27(0.59-8.67)
Employment: Yes	10 (15.4)	55 (84.6)	3.09 (1.36-7.04)*	5.35(1.49-19.20)*
Education: Secondary	26 (29.2)	63 (70.8)	0.67 (0.30-1.50)	
Diagnosis: Schizophrenia	7 (7.5)	86 (92.5)	21.68 (8.19-57.39)*	10.93(3.08-38.89)*
Insight: Good	6 (33.3)	12 (66.7)	0.78 (0.27-2.30)	
DAI: Positive	27 (29.0)	66 (71.0)	0.76 (0.25-2.30)	
GAF (mean, sd)	51 (7.0)	53.5 (11.7)	1.02 (0.98-1.06)	
SAPS (mean, sd)	8.0(3.3)	7.9 (3.4)	1.00 (0.89-1.12)	
SANS (mean, sd)	1.8 (3.4)	4.9 (5.8)	1.17 (1.05-1.31)*	1.31(1.06-1.62)*
Hopelessness: Yes	24 (28.6)	60 (71.4)	1.07 (0.43-2.67)	
BDI: Yes	5 (25.0)	15 (75.0)	1.2 (0.40-3.64)	
MHLC (internal): Yes	32 (29.6)	76 (70.4)	0.46 (0.16-1.30)	
MHLC (powerful others): Yes	32 (29.1)	78 (70.9)	0.51 (0.18-1.43)	
MHLC (chance) Yes	32 (29.6)	76 (70.5)	0.46 (0.16-1.30)	
Self-Consciousness: Yes	25 (27.5)	66 (72.5)	0.87 (0.39-1.90)	
Self-Consciousness(Private):Yes	25 (27.5)	66 (72.5)	0.86 (0.39-1.90)	
Self-Consciousness(Public):Yes	31 (33.3)	62 (66.7)	0.29 (0.11-0.76)*	0.07(0.01-0.55)*
Self-Consciousness (social anxiety): Yes	21 (27.3)	56 (72.7)	0.91 (0.43-1.94)	
QOL (Physical health) m,sd	12.7(2.9)	12.6(3.4)	0.99 (0.87-1.12)	
QOL (Psychological) m,sd	13.9(3.5)	14.3(2.9)	1.04(0.9-1.19)	
QOL (Social) m,sd	12.3(4.1)	13.8(3.8)	1.10(0.99-1.22)*	1.21(1.01-1.44)*
QOL (Environment) m,sd	12.0(3.4)	11.8(3.2)	1.0(0.86-1.11)	

Key: GAF: Global assessment for function level; BDI: Becks depression inventory; MHLC: Multidimensional Health Locus of Control; DAI: Drug Attitude Inventory; SANS: Scale for Assessment of Negative Symptoms; SAPS: Scale for Assessment of Positive Symptoms; QOL: Quality of life; *denotes statistically significant variable in Table 2.

and used in South Africa in similar population²⁴. Part of this tool (SCID 1) has also been used in Malawi to validate PHQ9 among patients with type-2 diabetes mellitus²⁵. Insight was measured using Birchwood scale²⁶, Drug attitude used Drug attitude inventory scale^{27,28}, symptoms were assessed using positive and negative symptoms of psychosis scales²⁹, and the level of functioning was measured using global assessment scale which is in SCID1²³. Data collection in the parent study was done by qualified Mental Health clinicians who were trained in all the data collection tools.

Data analysis

Data analysis was done using Stata 14 software released by Stata Corp in 2015³⁰. Descriptive statistics were summarized using frequencies and percentages. Logistic regression

test was used, statistical significance set at $\alpha=0.05$ for each variable tested to predict DUP. When using logistic regression test, dependent variable was DUP in months and independent variables referred to psychosocial and clinical factors. A logistic regression model was fitted to assess the association of clinical and psychosocial factors on DUP and results reported as odds ratio with 95% Confidence Interval.

Results

Social demographic characteristics of study participants

In this study we analysed all 140 participants. Most of the participants were male (60%, n=84) and single (51.4%, n=72). Median age of male participants was 31 years

(Range= 18 to 60 years), which was lower than females. Most participants had gone up to secondary school level (63.6%, n=89). Among the secondary school going participants, male participants were more (60.7%, n=54) than females. The proportion of unemployed participants was more than those that had reported to be employed in our study (53.6%, n=75).

In this study a diagnosis of either schizophrenia or schizoaffective disorder was made, and majority of the participants had a diagnosis of schizophrenia (66.4%, n=93). Male participants predominantly had a diagnosis of schizophrenia (64.5%, n=60).

Duration of untreated psychosis and social demographic

Duration of untreated psychosis in our study was categorized into two: less than 6 months and greater than 6 months; and greater than 6 months was regarded as long DUP⁹. In our study, mean DUP for the entire sample was 42 months (SD= ± 71 months, median=9.5 months, range= 0 to 320.5 months). Majority of the participants had longer DUP, (74%, n=103). Most male participants had longer DUP (73.8%, n=62) than females (see Table 2).

Factors predicting DUP in unadjusted and multivariate logistic regression

First, in unadjusted regression model, amongst all demographic variables, we found out that employment status predicted DUP, and age was slightly above the margin to predict DUP. Participants who reported to be employed were 3 times more likely to have long DUP in unadjusted logistic regression model (OR=3.09, 95% CI 1.36-7.04). There was statistically significant difference between those that were employed and the unemployed in the length of DUP.

Psychosocial factors included: hopelessness, psychological feelings of depression symptoms, multidimensional health locus of control (MHLC), self-consciousness and quality of life as perceived by participant. These psychosocial factors were categorized further into either 3 or 4 domains except hopelessness and depression which were dichotomized during analysis.

MHLC had 3 categories: a) Internal Health Locus of Control. b) Powerful Others Health Locus of Control, also known as External locus of control. c) Chance Health Locus of Control. Self-consciousness scale also had 3 categories: a) private, b) public, and c) social anxiety. Quality of life measured by WHOQOL-BREF, has 4 domains: a) physical health, b) psychological, c) social aspect of health, and d) environment.

Furthermore, in the unadjusted model, Participants who reported to have public self-consciousness were more likely to have long DUP (≥ 6 months) than those without public self-consciousness (OR=0.29, 95% CI 0.11-0.76). Our study results also shows that the participants' increase in the unit score on the social quality of life scale increased the likelihood for long DUP (OR=1.10, 95% CI 0.99-1.22).

With clinical factors in unadjusted logistic regression, participants who had a diagnosis of schizophrenia were 22 times likely to have long DUP (OR=21.68, 95% CI 8.19-57.39). Our findings also noted that participants' severity of negative symptoms was statistically associated with long DUP (OR=1.17, 95% CI 1.05-1.31). Other clinical factors were not significant in unadjusted regression model (see

table2).

However, when marital status, employment status, diagnosis, severity of negative symptoms, public self-consciousness, and social quality of life were included in a multivariate logistic model, and adjusted for age, they were still all shown to predict long DUP (see table 2).

Discussion

The mean DUP in our study is higher, 167.9 weeks (SD= ± 286.7), compared to other studies⁵⁵. We found employment status, diagnosis of schizophrenia, negative symptoms of psychosis, self-consciousness, and social quality of life to predict long DUP. The findings were independent of age when a multivariate logistic regression was run.

Socio demographic factors and Duration of untreated psychosis

In this study, among the socio demographic factors, employment was significantly associated with long DUP (see table 2). We found out that participants who were employed were more likely to have a long DUP (OR=5.35, 95% CI 1.49-19.20) as compared to those that were not employed. This is different with what Pek et al, found in their study that unemployed was associated with long DUP³¹. This difference can be possible in the study setting. This is because sometimes those that are employed, due to their engagement in their employment, the early (prodromal or subtle) symptoms of psychosis would be reported when they have an effect on functioning level. Rarely would the early symptoms be identified hence delay to report for consultation and prolonging DUP³². This also relates to the common presentation of psychosis as slow onset and early age of onset which has also been reported in other studies to be associated with DUP³³. Furthermore, in less acutely ill, as explained in a study by Tomita et al, patients may have experienced greater opportunity to choose their preferred practitioner, including traditional healers or general practitioners, therefore prolonging DUP³⁴. This could be similar in those that are employed, in their early stage of symptom presentation, they would not consult or take their time to consult or else opt for other quick consultations or counter medications until the symptoms are worse hence prolonging DUP.

Psychosocial factors and duration of untreated psychosis

First, participants that had public self-consciousness in this study were more likely to have a long DUP (OR=0.07, 95% CI 0.01-0.55) than those that had no public self-consciousness. This can be explained as a phenomenological concept of the disorder that an individual has when experiences the symptoms. Traditionally, the public and private aspects of self-consciousness have been investigated and measured since the 1970s, when developing the self-consciousness scale³⁵. There is not much studied on relationship between self-consciousness and DUP rather than reviews on how self-consciousness is related to psychotic disorders such as schizophrenia. However, it is one of the concepts that explain the phenomenology of psychosis such as schizophrenia. For instance, high levels of self-consciousness can either be associated with psychological well-being as well as psychological distress³⁶. This is usually described as the paradox of self-consciousness^{36,37}. Given this explanation, it is necessary to understand the concept of being aware of one's thoughts and beliefs and counterproductive aspects of self-

focus not being able to advance the critical thinking³⁵. This shapes on how an individual thinks about the public, such as thoughts over how the public views the individual with the disorder. Distorted thoughts of being viewed differently by the public can shape how an individual responds to the experiences of the illness. This therefore can make clients not seek consultation early consequently increasing DUP. This also can explain our finding in this study as relates to long DUP.

Another psychosocial factor which showed to predict DUP in our study was social quality of life. According to WHO Quality of life scale, the aspect of 'social health' also known as 'social relationship' constitutes personal relation, social support and sexual activity²⁰. In our study it was noted that an increase in score on 'social health' domain of 'WHO Quality of life' of participants was associated with long DUP. This is different with other study findings done in developed countries where it was noted that long DUP predicted poor objective 'Quality of life' perspectives in first episode psychosis^{38,39}. In a similar note with the current study, Malla et al, found that 'social relations' was inversely associated with DUP⁴⁰. Given this explanation, there is evidence for the association of 'social health' domain of 'quality of life' and DUP. In a study of measuring quality of life and outcome assessment in psychosis⁴¹ by Melle et al, similar findings to the current study were noted, poor global satisfaction was predicted by DUP of over 10 weeks. The association of 'social health' and DUP in the current study gives a notion that patients with first episode psychosis construct quality of life in a similar manner like other groups of people. It also clearly shows that those with longer durations of compromised function produces poor satisfaction with life rather than a downward readjustment of expectations.

Clinical factors and duration of untreated psychosis

In our study, there were two clinical factors that predicted duration of untreated psychosis: diagnosis of participant and the negative symptoms of psychosis. First, participants that had a diagnosis of schizophrenia were more likely to have a long DUP as compared to those that had a diagnosis of schizoaffective disorder. Most studies where DUP has been studied to relate with diagnosis of schizophrenia, has focused on the outcomes of either early intervention or delayed treatment which is not different with our study. Not strangely in this study that the diagnosis of schizophrenia was associated with long DUP considering the duration that an individual presents in order to make a diagnosis of schizophrenia, that is, at least 6 months of symptoms presentation or more according to Diagnostic statistical manual version 5⁴². The findings in this study are similar to what Haan et al, found that DUP as defined as delay in treatment with antipsychotic medication was significantly associated with the course of schizophrenia⁴³. Hui et al, in a study of DUP and clinical predictive factors also found that the diagnosis of schizophrenia was associated with long DUP which is similar to the findings in the current study⁴⁴. Given the association between diagnosis of schizophrenia and DUP, schizophrenia psychopathology has the potential of affecting an individual with the disorder to delay seeking help hence prolonging the DUP.

Further to this, we found out that schizophrenia symptoms, particularly negative symptoms of psychosis were found to be associated with long DUP in the current study. This is similar to other studies which noted the same association^{32,45}.

For instance, a meta-analysis done by Souabiby et al, showed that DUP is associated with negative symptoms, and it is associated with less severe negative symptoms when the DUP is shorter than 9 months⁴⁶. Furthermore, Haan et al,⁴³ also found that DUP was associated with negative symptoms in a study that was investigating DUP and outcome of schizophrenia. Similar to our study, in Nigeria also patients with predominantly negative symptoms were significantly more likely to have a long DUP³².

Barnes et al, in a study of DUP and social function-a one year follow up, also found that there was significant association between DUP and core negative symptoms score ($p=0.04$)¹⁰. In Barnes et al, study, when compared with positive symptoms of psychosis and negative symptoms, they were all associated with DUP¹⁰. This is different with our findings in this study where only negative symptoms were associated with DUP and not positive symptoms.

Furthermore, and contrary to the findings of the current study, other studies did not find association between negative symptoms and DUP (9). A DUP study that Addington et al, conducted in America, DUP study in a community treatment setting, did not find association between negative symptoms of psychosis and DUP⁹. This confirms that although most longitudinal first-episode studies have found that longer DUP is associated with severe positive symptoms, a positive association between DUP and negative symptoms has been found in some studies⁴⁷ and not other studies⁵. Similarly, Cechnicki et al, in a study of prognostic value of DUP in long term outcome of schizophrenia, there was no statistical significant association between negative symptoms and DUP apart from positive symptoms predicting DUP⁴⁸.

The differences or variations in the findings can be due to differences in relationship between DUP and different subgroups of patients with first episode psychosis. However, the association of negative symptoms of psychosis and DUP like in our study, can reflect either negative symptoms pre-dating onset and hinder help seeking or that long DUP itself leads to enduring negative symptoms. This can also be explained in the context of the nature of the negative symptoms that other people may not recognize early the need for consultation until significant deterioration is observed. For example, people with negative symptoms may not be violent a symptom which would prompt others to recognize the abnormality earlier rather than clients or a patient who would just withdraw, reduce in activities performance, psychomotor retarded in the daily functioning, of which in a way they look more of passive symptoms than positive symptoms⁴². This can actually make or enhance delays because people would still regard such type of patients not problematic and that can be taken for consultation at a later time. Furthermore, negative symptoms of psychosis may be believed and associated with cultural beliefs in some African communities that a person has been bewitched hence delaying further for appropriate intervention³². This is also highlighted in a study done in Nigeria³², where the findings are similar to our study.

Implications of the study

Our study highlights the need to target factors that predict DUP to have good treatment outcome. Integration of mental health care in the already existing health programs such as in clinical practice or community health to enhance early identification of those that are having early symptoms of psychosis and refer or help accordingly. Community mental

health programs can help in illness awareness and defining the pathways to care. When there is delay in symptom identification, the psychopathology of the disorder will hinder an individual to realise the need for consultation and help hence increasing the DUP consequently poor outcome at the late stage of the disorder. This is also echoed by Norman et al, that efforts to decrease delay in treating individuals with clear established psychotic disorders are justified⁸. This is not just by the immediate reduction in symptoms but by potential improvement in the outcome⁸. Given this explanation, psycho education programmes particularly on the signs and symptoms of psychotic disorder to people either those that identify themselves as clients or not is an ideal way to advocate for early intervention. One of the ultimate goals for the early intervention services should be to identify the first episode psychosis early and start effective treatment.

Study limitations

Our study was done in one region, therefore there could be differences in the cultural understanding of mental illness and bring in variation in the time that people take to seek help and treatment. Furthermore, the cultural beliefs may differ between regions and also affect on how that can predict the DUP. Therefore, it would be encouraged also to consider exploring the DUP and its predictors in other settings with different cultural background which can give a picture of a national representation on the burden of the problem.

Conclusion

Most clients with psychosis have long DUP and it is important to consider targeting the clinical and psychosocial factor to reduce the poor outcomes of long DUP. Integration of mental health care services has been highlighted to enhance awareness and improve pathways to care. Further study in factors that predict DUP has been recommended to be done in other region to look at variations of the burden.

Conflict of interest

There is no conflict of interest to all authors in this manuscript.

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