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PERSPECTIVE

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EDITORIAL

THE NEED FOR A RADICAL TRANSFORMATION OF THE HEALTHCARE SYSTEM IN ETHIOPIA: EXAMPLES FROM MENTAL HEALTH RESEARCH

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We ignore mental disorders at our own peril. Six of the leading 20 causes of the global disease burden are mental and behavioural disorders, with depression topping the list as the second leading cause (1). In Ethiopia, extensive knowledge about mental disorders and their impact has been gained from scientific observations since the establishment of modern mental healthcare in the country. These studies have involved diverse population groups: women, children and adults; general populations, social isolates, displaced people and the homeless. Overall, four generation of studies may be distinguished. The first-generation studies were conducted primarily in health facilities and involved interviews by psychiatrists. The second-generation studies were mainly population based and used screening tools administered by lay interviewers.

The third-generation studies constituted a major methodological advance and employed structured diagnostic interviews administered by clinicians. The latter studies were particularly relevant for the understanding of psychotic disorders. Through these three generation of studies it was possible to make a strong public health case for mental disorders: that mental disorders are common, serious, but treatable. The Butajira project on severe mental disorders (schizophrenia, bipolar disorder and severe depression) is arguably the most important study in relation to disease conditions, scope and impact (2). One of the notable outputs of this study was the demonstration that people with schizophrenia, depression and bipolar disorder die about three decades prematurely compared to the rest of the population (3).

The fourth-generation studies involved clinical trials, complex interventions and neurobiological studies. The complex intervention studies attempted to model innovative, safe and scalable care approaches to ensure quality mental healthcare in primary care settings. Two studies that may be considered a fourth-generation studies are published in the current issue of the Ethiopian Medical Journal (4,5).

Understanding and dealing competently with multi-morbidity is the linchpin of a modern health service anywhere in the world. Depression has emerged as an important co-morbid condition with both communicable and non-communicable diseases in developed as well as developing countries. For example, a study among patients with tuberculosis in Ethiopia has demonstrated not only strong co-morbidity between depression and tuberculosis but very serious consequences arising from such comorbidity (6). Patients with tuberculosis and co-morbid depression at entry to care were prospectively at a significantly increased risk for premature mortality, disability, poorer quality of life and treatment default. The high comorbidity between hypertension and depressive symptoms reported by Abraham T., et al. and Fekadu A. and Alem A, in this issue (4,5), while not surprising, should raise concerns.

Non-communicable diseases (NCDs) have become major public health problems in Ethiopia. According to the recent report by the Ethiopia NCDI Commission, 43.5% of mortality in Ethiopia was related to NCDs. Hypertension is of particular concern. It has high prevalence in Ethiopia, and is also an important risk factor for other NCDs (7). Alarmed by the high prevalence, some have referred to hypertension as the “silent epidemic” (8). Admitted that the high prevalence of depression in people with hypertension may in part be due to the use of a symptom checklist, the article rightly highlights the challenges of the modern health system -detecting co-morbidity and providing adequate quality care when detected. Nothing short of a drastic transformation of the healthcare system of Ethiopia is required if it is to be fit for the 21st century health needs of the country.

The second paper in this issue (5) highlights the gaps in the healthcare system in relation to caregiver burden

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among carers of people with psychosis. Informal caregivers are the backbone of healthcare in developing countries. While most caregiving will arise from other NCDs, severe mental illnesses can make caring more difficult. The lack of social care and the virtual absence of biomedical care in most parts of the country makes caring more challenging. Using a comprehensive assessment tool that evaluated a range of experiences linked to caring, the study showed a high level of burden related to a range of care experiences. Despite the high level of burden of care, caregivers rarely wanted 'out'. Their utmost concern was the wellbeing of the patient. This is more inspiring considering the virtual absence of social care programmes, the extreme inadequacy of biomedical care and the little support from informal providers, such as Non-Governmental, religious and community organisations (9). While this is a testimony to the fact that 'unsung' heroes live almost in every household, this status quo is unacceptable. What is the implication of these two studies for healthcare in Ethiopia? The studies are a window into the need for a radical transformation of the healthcare system. First, the acute care model, that is pervasive in the current health system is not fit for purpose.

Multimorbidity, co-occurrence of two or more chronic conditions, is the reality of modern healthcare. For example, at least one in four people in the United Kingdom and United States of America have multimorbidity, with two-thirds of those aged 65 and above having multimorbidity (10.11). Adopting the chronic care model, instead of the prevailing acute care model, would help in addressing key comorbidities, such as depression, that affect quality of life and disease outcomes adversely. The personalised and continuous engagement in the chronic care model would also increase the possibilities for detection of co-morbid depression. The recent increase in the number of medical graduates, combined with the requirement for continuous professional development, offer a platform for substantive quality improvement.

Innovations to engage and support informal caregivers is also an urgent priority. If not for the sake of the caregivers, the changing socio-demographics, economics and culture demand changing the way healthcare systems extend support to caregivers. A chronic care model requires a 'community' approach to healthcare. This means empowering not only the patients but also the caregivers. The 'respectful' and 'compassionate' care agenda that engages the patient and carer is essential. This also calls for engaging the rich community resources that are currently little appreciated and deployed. It is also noteworthy that highly infectious diseases, such as the COVID-19 and tuberculosis, also demand a new approach to caregiver engagement. A serious commitment to improving the quality of care requires a serious commitment to transforming the current care model drastically.

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ORIGINAL ARTICLE

TREATMENT GAP FOR CO-MORBID DEPRESSION IN MEDICAL OUTPATIENTS WITH HYPERTENSION: A CROSS-SECTIONAL HOSPITAL-BASED STUDY

Teklu Abraham, MD[1], Solomon Teferra, MD, PhD[1], Tesfaye Yilma, MD[2], Charlotte Hanlon, MRCPsych, PhD[1,3,4*]

ABSTRACT

Introduction: *Despite an increasing number of studies reporting high levels of co-morbidity between depression and hypertension in high-income countries, there is limited information on co-morbid depression among hypertensive patients in low- and middle-income countries.*

Objectives: *The aim of this study was to determine the prevalence of depression, associated factors and treatment gap among hypertensive patients attending outpatient follow-up at a referral hospital in Ethiopia.*

Methods*: A hospital-based cross-sectional study was conducted in 302 consecutive outpatient attendees with hypertension. Probable depression was measured using an interviewer administered depression scale (the Patient Health Questionnaire; PHQ-9) previously validated for the Ethiopian setting for a cut-off of 9 and above. Contextualised standardized measures of medication adherence, alcohol and khat use were used. Clinical information was extracted from medical notes, augmented by assessment of body mass index. Univariate and multivariable analyses were carried out to assess factors associated with depression.*

Results*: The prevalence of probable depression among participants was 22.2%. The treatment gap was 91%. Only 9% (n=6) had received any treatment for depression. Of these, all were prescribed an antidepressant. Female gender, adjusted odds ratio (aOR) 2.6, (95% confidence interval (CI) 1.2, 5.8), being unmarried (aOR 2.0; 95% CI 1.0, 3.7) and having two or more co-morbid medical illnesses (aOR 12.6; 95% CI 4.3, 37.0) were associated independently with depression. There was no association between depression and medication adherence, diet, physical activity or body mass index.*

Conclusions*: The prevalence of depression is high among hypertensive outpatients in Ethiopia. Most of the depressed hypertensive patients were not receiving treatment for depression. Larger, prospective studies are needed to further evaluate the impact of co-morbid depression on patient behaviours and hypertensive complications. Training general health workers to detect and treat co-morbid depression, as per recommendations from the World Health Organization is essential to decrease the treatment gap.*

Key words*: Depression, Hypertension, Prevalence, Co-morbid, Ethiopia, treatment gap*

INTRODUCTION

Depression and hypertension are among the leading causes of the global burden of disease (1, 2). Growing evidence suggests high levels of co-morbidity between hypertension and depression (3). The overall prevalence of depression in people with hypertension was estimated to be 26.8% (95% Confidence Interval (CI): 21.7%-32.3%) in a systematic review and meta-analysis of 41 observational studies from high-income countries (HICs) (4).

Several pathophysiological mechanisms have been proposed to explain the complex interaction between the two conditions, including autonomic nervous system dysfunction, shared genetic vulnerability, behavioral and psychosocial factors (5).

Depression has been found to increase the incidence of hypertension (6). In keeping with this, depression was found to be associated with subsequent diagnosis of hypertension in the World Mental Health Survey (WMHS), comprising 19 countries (7). Hypertension may also increase the risk of depression. There is now compelling evidence that the antihypertensive medications reserpine and methyldopa can induce or worsen depression, but the data supporting the link between beta-blockers and depression are not as certain (8, 9). The association between depression and hypertension has not been so clearly determined in studies from low- and middle-income countries (LMICs) to date. A population-based study from sub-Saharan Africa (3) and a prospective population-based study in Brazil (10) reported an absence of any association between hypertension and depression.

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Depression in people with hypertension has been associated with various socio-demographic characteristics (older age, female sex (11), low education (11,12), unemployment, being unmarried (12,13), clinical characteristics (having multiple co-morbid chronic diseases (3), potentially detrimental behaviours (cigarette smoking (5,11), alcohol intake (5), poor adherence to antihypertensive medications (11,13) and physical inactivity) and possible adverse clinical consequences, for example, uncontrolled hypertension (14). Despite this, the burden of depression in clinical settings in LMICs has been little-investigated. Recent global movements to expand access to mental health care integrated within general healthcare settings (15) offer great potential to address the burden of untreated depression in medical settings, including people with hypertension.

In Ethiopia, the prevalence of depression was estimated to be 9.1% in a nationally representative survey (16) and it was in the top 10 causes of disease burden (17). In a recent meta-analysis, hypertension was estimated to affect 19.6% of Ethiopians aged 15 years and older (18). Early detection and provision of effective treatment for co-morbid depression would be expected to bring about better clinical outcomes for both disorders (7). However, as a prerequisite to integrating depression care, it is imperative to understand the current burden of depression in such settings and the level of unmet need for mental health care.

This study aimed at determining the prevalence of co-morbid depression, associated factors and the treatment gap among people with hypertension attending medical outpatient clinics at a government referral hospital in Addis Ababa, Ethiopia.

PATIENTS AND METHODS

Study design: A hospital-based cross-sectional study was conducted in July 2016 at Zewditu Memorial Hospital (ZMH), a general referral hospital located in the capital city Addis Ababa, Ethiopia. ZMH has 188 in-patient beds and serves 9,171 inpatients and 89,540 outpatients per year (19). People with hypertension are seen by a case team consisting of an internist and three nurses at a hypertension clinic twice a week. The clinic provides outpatient follow up services for adults diagnosed with hypertension who have been referred from the different departments of the hospital and nearby health centers. Currently there are around 720 patients under regular follow up at the clinic, with an average of 30 patients seen on each clinic day.

Sample Size: The sample size was estimated using the single population proportion formula with 95% confidence level and 80% power.

As the prevalence of depression among hypertensive patients is not known in Ethiopia, the 26.8% prevalence reported in a meta-analysis of observational studies (7) was used. With these assumptions, a sample size of 302 was required.

Sampling: The study included all consenting patients aged 18 years and above with an established diagnosis of hypertension who attended for follow up at ZMH hypertension clinic during the study period. Acutely unwell patients, those with cognitive impairment and patients who were unable to communicate in the language of the interview (Amharic) were excluded from the study. Consecutive hypertensive patients who fulfilled inclusion criteria were included until the target sample size was obtained.

Measures: The data were collected by a trained nurse and a psychiatric resident using a structured questionnaire. Participants were interviewed and information regarding socio-demographic characteristics, behavioral factors and clinical characteristics were collected.

Depression was assessed using the PHQ-9 (20). The PHQ-9 is a nine-item instrument with four response options. It assesses various domains of depressive symptoms and quantifies their severity in the past two weeks. PHQ-9 has been validated in Ethiopia and was found to be a reliable and valid instrument to assess depression among adults in an outpatient health care setting. An optimal cut -off score of ≥9 to define probable depression in medical out-patients in Ethiopia has been proposed (21).

Clinical measures: Height and weight were measured by a nurse. Body mass index (BMI) was calculated and categorized as normal (<25 kg/m^2), overweight (25-29.9kg/m^2) and obese (≥30 kg/m^2) according to the WHO classification (22).

Blood Pressure was extracted from the medical notes for the current clinic attendance. Participants with a systolic blood pressure ≥ 140 mmHg or a diastolic blood pressure ≥ 90 mmHg were classified as having uncontrolled blood pressure. All medications being taken at the time of data collection were recorded from the medical records and categorized according to their number and pharmacological class. Adherence was assessed using a 4-item measure of medication adherence (23) which has been adapted for Ethiopia previously (24). The total score was classified as high (0), medium (1-2) and low (3-4) adherence.

Participants were asked for any previous diagnosis of chronic medical conditions, including diabetes mellitus, heart disease, chronic respiratory diseases/ asthma, HIV/AIDS, cancer and epilepsy.

Lifestyle measures: Physical activity was classified as regular activities carried out at least twice a week during leisure time or as a part of work. Three or more servings of fruit and vegetable per week were classified as a high fruit and vegetable diet (25). Participants using any tobacco product at the time of data collection were classified as smokers. Frequency of khat use (amphetamine-like stimulant) was recorded.

Alcohol use was assessed using the FAST Alcohol Screening Test (26). The FAST has been adapted for use in Ethiopia (27) and an overall total score of 3 and above was classified as hazardous use.

Data analysis: Data were entered and analyzed using SPSS software version 20. Descriptive statistics was computed for socio-demographic, clinical and behavioral characteristics of participants. Chi-squared and Fisher's exact test were used for the purpose of statistical comparisons. Univariate and multivariable regression analysis were carried out for effect estimation. A priori explanatory variables to be included in the multivariable model were: sex, age, marital status, educational status, number of co-morbid chronic illnesses, taking beta blocker medication, alcohol use, BMI, physical activity, adherence with medication, duration of diagnosed hypertension and uncontrolled diastolic blood pressure. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. A value of $p < 0.05$ was considered statistically significant.

Ethics, consent and permissions: Ethical approval was obtained from the Scientific Review Committee, Department of Psychiatry, Addis Ababa University and Addis Ababa City Administration Health Bureau before conducting the study. Written, informed consent was obtained and confidentiality was maintained. Any person identified with depression was referred to the hospital psychiatric out-patient clinic for further assessment treatment. Adherence counseling was given for patients with poor treatment adherence.

RESULTS

Socio-demographic characteristics: A total of 302 participants were included in this study. The majority of participants (57.0%) were female. The age ranged between 18 and 96 years, with a mean of 55.8±12.9 years. More than a third (34.1%) of participants belonged to the age group 50-59 years.

Over a quarter (25.2%) of participants had at least college level education, but 60 (19.9%) had no formal education. More than two thirds (67.5%) were married. Around half of the participants (44.0%) were either employed or merchants and 36 (11.9%) were unemployed (Table 1).

Table 1: Socio-demographic characteristics of patients on treatment for hypertension, Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2016 (n=302)

Characteristics	Number	Percent
Sex		
Male	130	43.0
Female	172	57.0
Age group (years)		
18-29	7	2.3
30-39	24	7.9
40-49	50	16.6
50-59	103	34.1
60-69	72	23.8
≥70	46	15.2
Educational level		
No Formal education	60	19.9
Grade 1-6	52	17.2
Grade 7-12	114	37.7
College/above	76	25.2
Marital status		
Unmarried	98	32.5
Married	204	67.5
Job status		
Unemployed	36	11.9
Employed/merchant	133	44.0
Housewife	50	16.6
Other	83	27.5

Clinical and behavioral characteristics: The mean systolic and diastolic blood pressures were 142.7 (Standard Deviation (SD) 22.9) mmHg and 83.3 (SD 12.4) mmHg, respectively. Diastolic blood pressure was uncontrolled (≥90 mmHg) among 42.4% (n=128) and systolic blood pressure was uncontrolled (≥140 mmHg) among 56.6% (n=171) of the participants. The mean duration of diagnosed hypertension among the participants was 10.1 (SD 8.7) years. Enalapril 162 (53.6%), nifedipine 153 (50.7%) and atenolol 118 (39.1%) were the commonest antihypertensive medications prescribed to participants.

Nearly a quarter of participants (23.2%; n=68) were taking three or more antihypertensive medications.

The most commonly used classes of antihypertensive medications were calcium channel blockers (56%; n= 169), angiotensin converting enzyme inhibitors (54.6%; n=165), beta-blockers (42.4%; n=128)) and diuretics (26.8%; n=81).

Half (50.0%) of the participants had at least one other chronic medical illness. Twenty-three (7.7%) had two or more co-morbid medical conditions. (Table 2).

Table 2: Clinical characteristics of people receiving treatment for hypertension, Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2016 (n=302)

Characteristics	Number	percent
Duration of diagnosed hypertension		
<2 years	39	12.9
2-5 years	76	25.2
>5 years	187	61.9
BP (mmHg)		
<140/90	104	34.4
Diastolic Blood Pressure ≥90	128	42.4
Systolic Blood Pressure ≥140	171	56.6
Medications		
Propranolol	8	2.6
Atenolol	118	39.1
Metoprolol	3	1.0
Amlodipine	17	5.6
Nifedipine	153	50.7
Hydrochlorothiazide	81	26.8
Enalapril	162	53.6
Captopril	3	1.0
Medications for diabetes mellitus	81	26.8
Aspirin	11	3.6
Statins	18	6.0
Antihypertensive medication class		
Diuretics	81	26.8
Beta blockers	128	42.4
ACE inhibitors	165	54.6
Calcium channel blockers	169	56.0
Number of antihypertensive medications		
0	31	10.3
1	71	23.5
2	130	43.0
3	66	21.9
4	4	1.3
Chronic medical conditions		
Diabetes mellitus	82	27.2
Heart diseases	21	7.0
Respiratory system diseases	22	7.3
HIV/AIDS	6	2.0
Cancer	1	.3
Renal diseases	35	11.6
Others	9	3.0
Number of chronic diseases		
0	151	50.0
1	128	42.4
2	21	7.0
3	2	.7

Two thirds (66.6%) of the participants had high adherence (MMAS-4 score=0) with their antihypertensive medications. The mean (SD) Body Mass Index of participants was 26.6 (4.9) kg/m^2. More than a third (35.8%) of participants were overweight and 24.5% were obese. Only a quarter (23.5%) of participants had three or more servings of fruits and vegetables a week.

The majority (64.6%) reported doing regular physical activity. Very few (3.0%) of the participants were current smokers and 37 (12.3%) had hazardous use of alcohol (FAST score ≥3). Ten (3.3%) reported current khat use and 187 (61.9%) reported current coffee consumption. (Table 3).

Table 3: Behavioural characteristics of participants, Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2016 (n=302)

Characteristics	Number	Percent
Adherence to medication		
Low (MMAS-4 ≥3)	3	1.0
Medium (MMAS-4 =1 or 2)	98	32.5
High (MMAS-4 =0)	201	66.6
BMI (kg/m2)		
<25	120	39.7
≥25 and <30	108	35.8
≥30	74	24.5
Physical activity		
No	112	37.1
Yes	190	62.9
Fruits/vegetables ≥3servings/week		
No	231	76.5
Yes	71	23.5
Coffee consumption		
No	115	38.1
Yes	187	61.9
Hazardous alcohol use (FAST ≥3)		
No	265	87.7
Yes	37	12.3
Smoking		
No	293	97.0
Yes	9	3.0
Khat chewing		
No	292	96.7
Yes	10	3.3

Prevalence of depression and treatment gap among participants: The mean (SD) PHQ-9 score for all participants was 4.5 (4.9). The prevalence of depression (PHQ-9 score ≥9) among participants was 22.2% (n=67).

Only six participants (8.9%) were receiving treatment for depression, of whom all were receiving pharmacological treatment and none had received a psychosocial intervention. Four were treated for depression in public hospitals, one in a health center, and the other in a private general clinic.

Univariate associations with depression: In the univariate analyses, female gender (OR 2.1, 95% CI 1.2, 3.7), being unmarried (OR 2.0, 95% CI 1.1, 3.5), taking a beta blocker antihypertensive (OR 1.8, 95% CI 1.1, 3.1), physical inactivity (OR 1.9, 95% CI 1.1, 3.3) and having two or more co-morbid medical illnesses (OR 8.2, 95% CI 3.2, 21.2) were associated with depression. (Table 4)

Table 2: Clinical characteristics of people receiving treatment for hypertension, Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2016 (n=302)

Characteristics	Number	percent
Duration of diagnosed hypertension		
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HIV/AIDS	6	2.0
Cancer	1	.3
Renal diseases	35	11.6
Others	9	3.0
Number of chronic diseases		
0	151	50.0
1	128	42.4
2	21	7.0
3	2	.7

In the multivariable model, female gender (adjusted odds ratio (aOR) 2.6, 95% CI 1.2, 5.8), being unmarried (aOR 2.0, 95% CI 1.0, 3.7) and having two or more co-morbid medical illnesses (aOR 12.6, 95% CI 4.3, 37.0) were associated independently with increased odds of depression among participants.

Taking beta blocker became marginally non-significant in the multivariable analysis but with the strength of association unchanged. Age, level of education, medication adherence, alcohol abuse, BMI, duration of diagnosed hypertension and blood pressure control showed no association with depression (Table 5).

Table 5: Multiple logistic regression analysis of factors associated with depression among people on treatment for hypertension, Zewditu Memorial Hospital, Addis Ababa, Ethiopia, 2016 (n=302)

Characteristics	Association with PHQ score ≥ 9	
	Unadjusted Odds Ratio (95% CI)	Adjusted Odds Ratio (95% CI)
Sex (female)	2.07 (1.16-3.70)	2.63 (1.20-5.80)
Age (years)	1.01 (0.99-1.03)	1.01 (0.98-1.04)
Education level (years of schooling)	0.99 (0.94-1.04)	1.03 (0.97-1.10)
Marital status (unmarried)	1.99 (1.14-3.48)	1.95 (1.02-3.71)
Number of co-morbid chronic diseases		
0	Reference	Reference
1	1.55 (0.85-2.83)	1.68 (0.87-3.22)
≥2	8.23 (3.20-21.16)	12.58 (4.28-36.97)
Beta blockers (present vs. absent)	1.81 (1.05-3.12)	1.88 (1.00-3.56)*
Hazardous alcohol use (FAST ≥3)	1.35 (0.62-2.96)	2.70 (1.00-7.30)±
BMI (kg/m2)		
<25	Reference	Reference
25-29.9	1.34 (0.71-2.55)	1.30 (0.62-2.74)
≥30	1.65 (0.83-3.29)	1.23 (0.55-2.72)
Physical inactivity	1.92 (1.12-3.32)	1.73 (0.91-3.31)
Adherence (low/medium)	1.73 (0.99-3.02)	1.66 (0.89-3.12)
Duration of diagnosed hypertension (years)	1.03 (1.00-1.06)	1.03 (0.99-1.07)
Uncontrolled DBP	1.13 (0.66-1.96)	1.04 (0.56-1.93)

*p = 0.05; ±p = 0.05; PHQ = Patient Health Questionnaire; FAST = FAST Alcohol Screening Test; BMI = Body Mass Index; DBP = Diastolic Blood Pressure; SBP = Systolic Blood Pressure

DISCUSSION

Prevalence of depression: In this hospital-based study from Ethiopia, the prevalence of depression was high at 22.2%. Although we did not have a comparison group in our study, this is substantially higher than the 9.1% 12-month prevalence reported among the general population in the 2012 Ethiopian National Health Survey (16). Increased prevalence of depression in hypertensive patients has been described in previous studies (12, 28). In a hospital-based study from Nigeria, the prevalence of depression among participants with essential hypertension was 26.7% (12). In another study that compared prevalence of depression among hypertensive patients and their age matched healthy controls, hypertension had a significant positive relationship with depression (28). The prevalence of depression in our study is also comparable to the 26.8% (95% CI 21.7, 32.3) overall prevalence of depression among people with hypertension reported in a recent meta-analysis from HICs (4).

Despite affecting nearly one quarter of hypertensive out-patients in our study, 91% were not receiving treatment for co-morbid depression. In a study that reviewed community-based psychiatric epidemiological studies that used standardized diagnostic instruments, the median treatment gap was 56.3% for depression, but data were lacking from LMICs (29). The treatment gap in this study is as high as the treatment gap for mental disorders observed in a rural Ethiopian population with limited access to mental health care (30).This is surprising given the presence of an on-site psychiatric clinic and the skilled levels of clinicians, including general and specialist physicians, present in this referral hospital. This might be due to low patient and provider awareness about depression and its treatment.

Factors associated with depression: In this study, having two or more co-morbid chronic medical illnesses was associated with increased odds of depression, both in univariate and multivariable analyses. This may be due to increased disability and decreased quality of life caused by additive effect of multiple co-morbid illnesses. Treatment of co-morbid chronic medical conditions could be considered as a potential target to reduce depression among hypertensive patients.

Despite the majority of patients taking two or more antihypertensive medications, nearly half of the participants in this study had uncontrolled blood pressure which might have contributed to increased risk of co-morbidities, caused by complications of high blood pressure, and disability. It might also reflect the quality of chronic disease care in the Ethiopian setting, where the health system and patient and provider expectations are orientated to acute, curable infectious conditions rather than long-term care.

Taking beta blocker antihypertensive medication was associated significantly with depression in univariate analysis. The association became marginally non-significant in the multivariable analysis (aOR=1.88, 95% CI= 1.00-3.56). This finding may reflect a true association between beta blockade and depression that was not evident due to small sample size. The association between beta blockers and depression has been supported in previous studies. Luijendijk et al. conducted a cohort study that included 5104 elderly persons to examine the relationship between beta-blockers and incident depression. They found that lipophilic beta blockers were associated with an increased risk of depressive symptoms (9).

Depression and behaviors: Medication adherence was not significantly associated with depression in this study. This finding was in agreement with a previous study that reported no significant association between poor treatment adherence and presence of depression among subjects with hypertension (13). However, the same study found significant association between poor treatment adherence and severity of depression which was not assessed in the present study. Contrary to our finding, a meta-analysis of twelve studies reported that depression is significantly associated with poor treatment adherence in patients with chronic medical illnesses (31). This difference may be due to methodological factors. In this study, we relied on self-report of medication adherence and the percentage of participants reporting poor adherence was low. The sample itself is biased towards people who have continued to engage with treatment, and were relatively well-educated, which may mean that this finding is not generalizable to the rest of the population.

Sedentary lifestyle has been previously reported to be associated with depression among hypertensive patients (13). We found that physical inactivity was associated with depression in univariate but not in multivariable analysis. The heterogeneity of the population attending ZMH might have contributed to this finding. Some of the attendees were from Addis Ababa, well-educated and not in manual jobs, while others were farmers referred for refractory blood pressure from outside of the city.

The association between depression and exercise is only really relevant for the people from Addis Ababa, but we did not have an adequate sample size to explore this hypothesis in our dataset. Other factors known to affect the beneficial effects of exercise on depression such as intensity of exercise (32), social support and resilience (33) need to be explored.

Contrary to previous studies (11,33), hazardous alcohol use was not associated with depression in our study. This might be due to under-reporting of alcohol use by participants.

Limitations: This study was a cross-sectional hospital-based study. Its findings may not be generalizable to the entire population of hypertensive patients. No causal links or directions can be inferred in a cross-sectional survey of this nature. The study used a sample size calculated for measurement of prevalence. A larger sample size would be preferable for measures of association and adjusting for confounders. Additionally, khat and tobacco use were not included in the final logistic analysis because of the small proportion of users in the current sample.

Conclusions: The findings of this study suggest a need to equip general health workers to detect, assess and treat co-morbid depression in people with hypertension in Ethiopia. A prospective study with a larger sample size is needed for future studies to establish more definitive link between depression and hypertension and consequences of co-morbid depression on patient behaviours and hypertension complications. Furthermore, future studies looking at the effect of physical activity and beta-blockers on depression are needed to understand the nature of their relationship.

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Competing of interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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ORIGINAL ARTICLE

LIVING WITH HIGH BURDEN OF CARE: EXPERIENCE OF CAREGIVERS OF PEOPLE WITH SEVERE MENTAL ILLNESS IN RURAL ETHIOPIA

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ABSTRACT

Introduction*: Caregivers of people with severe mental illness experience substantial burden from providing care. This burden is likely to be higher in low- and middle-income countries where statutory medical and social services are in low supply.*

Objective: *We conducted a study aiming to evaluate the level of caregiver burden among caregivers of people with severe mental illness.*

Methods*: The study was population-based cross-sectional evaluation carried out in the Sodo district of the Gurage zone in south Ethiopia. Three hundred people with severe mental illness and matched caregivers were included. The involvement evaluation questionnaire, a widely used tool for assessing caregiver burden, was administered. The involvement evaluation questionnaire has four domains (urging, worry, supervision and tension).*

Results*: Caregivers were predominantly women (52.5%), married (67.6%), under 45 years of age (57.5%) and had little or no formal education (60.9%). The overall mean burden score (95% confidence interval (CI)) was 45.3 (43.2, 47.4); highest for "urging" (mean=15.5; 95% CI=14.6, 16.4) and "worrying" domains (mean=13.7; 95% CI=12.9, 14.4). Being female caregiver, first degree relative, experiencing distress and caring for patients with higher levels of symptomatology and disability were significantly associated with higher overall burden score.*

Conclusions: *As anticipated, caregivers in this setting have higher levels of burden of caring compared with care givers in Europe and other settings. Interventions should aim not only at decreasing patient symptoms and improving functionality, but also at decreasing caregiver distress focused on women and first-degree relatives.*

Key words: Burden of care, Caregivers, Mental Illness, Ethiopia

INTRODUCTION

Severe mental illnesses (SMI), such as schizophrenia and mood disorders with psychotic features, often result in substantial burden on patients and those providing care for them (1). For those providing care, the experience may be both positive and negative. The positive experience relates to the satisfaction and self-esteem caregivers may feel due to providing care, whereas the negative impact may result from the dissatisfaction and distresses that the caregiver may perceive related to caregiving (2).

These negative experiences are often referred to as burden (3), signifying the presence of problems, difficulties or adverse events affecting the lives of the members of patients' family (4).

Burden could also be understood as objective or subjective. Objective burden is related to the negative impact of caregiving on the caregiver's routine activities and subjective burden referring to the emotional impacts (5).

"Caregiver consequences" is a more neutral term that comprises both the negative and positive aspects of caregiving (1); however, the terms caregiver burden and consequences are often used interchangeably.

While the level of burden due to providing care is generally high (6,7), the level is relatively higher among caregivers of patients with SMI than that of caregiver's of patients with chronic medical conditions (8). Moreover, the burden is also likely to be higher in low and middle income countries (LMICs) like Ethiopia, where statutory medical and social services are unavailable or in short supply and people with SMI obtain most of the care they need from their families (6).

To our knowledge very few studies have been conducted in Ethiopia or other LMICs pertaining to caregiver burden. Those studies used Family Burden Interview (FBI), a measure of objective burden (6), and reported considerable level of burden, particularly related to finances,

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among caregivers of patients with SMI. A subsequent follow-up study (9) indicated that care giver burden does improve over time although this was more likely among in care providers of patients whose symptoms have improved or were experiencing sustained remission.

The aim of the present study was to evaluate the consequences of caregiving among caregivers of people with SMI using a tool that assesses both subjective and objective burden of caregiving. The study also aims to identify illness related and sociodemographic correlates of caregiver consequences. We hypothesized that caregivers of people with SMI experience higher levels of burden and that as disability and symptom severity increases caregiver burden increases.

PATIENTS AND METHODS

Study setting and design: The study was a population-based cross-sectional survey of patients with SMI and matched caregivers conducted in the Sodo district of the Gurage Zone in Ethiopia. The capital city of the district, Bui, is located about 100 km from Addis Ababa. At the time of the study, the district had 58 sub-districts, four urban and 54 rural, and the population of the district was about 170,000. Healthcare was provided by one primary hospital, eight primary health centers and 58 health posts.

***Participants*:** Participants were recruited from December 2014 to July 2015. Patients were first identified and then matched with a caregiver, who would have typically accompanied the patient. Caregivers were invited explicitly to accompany the patient during the day of assessment. This was possible because of the case identification and referral processes that were in place for the study. If the appropriate caregiver (inclusion criteria below) had not accompanied the patient, they were given another appointment to do so.

Patients with SMI were identified through a two-stage process. First, potential cases with psychosis were identified and referred by community key informants, consisting of health extension workers and community leaders trained for half a day by a psychiatrist with experience in training key informants. Second, these potential cases were referred to the health centres where trained psychiatric nurses conducted a semi-structured interview to confirm diagnosis and evaluate other clinical parameters, such as symptom severity. To be included in the study, participants had to be at least 18 years of age, fulfil diagnostic criteria of the International Classification of Diseases (ICD) for one of the major psychotic disorders (ICD-10 F20 and ICD-10 F30 [psychotic subsections]), be in need of mental health care at the time of detection, and were resident in the area for at least six months. The inclusion criteria for caregivers were; age 18 years and above, being a primary carer of a patient with SMI and that the carer is not being paid for providing the care, i.e., were informal caregivers.

Sample size: Three hundred carers providing care for 300 patients who have received a diagnosis of SMI were recruited to take part. All consenting participants during the study period were included and no formal assessment of sample size was carried out. However, the sample size was adequate for the aims of describing the levels of carer burden and to assess key factors that may be associated with the burden.

Measures: Socio-demographic information of the patients including their age, gender, ethnicity, marital status, religion, educational background, employment status, relative wealth and residence was collected. Moreover, other instruments that assesses the clinical, social, physical and psychological parameters were administered.

Trained psychiatric nurses administered the clinical assessment instruments whereas the other instruments were administered by trained and experienced lay data collectors. We used the Amharic version of the Involvement Evaluation Questionnaire (IEQ) to measure the burden of caregivers of people with psychotic disorder. Some of the instruments used are summarized below.

OPCRIT (Operational Criteria for Research): is an operational criteria checklist for psychotic and affective illnesses. It was used in this study to confirm clinical diagnosis of SMI. OPCRIT has proven reliability to diagnose large number of mental disorders (10).

Brief Psychiatric Rating Scale- Expanded version (BPRSE): is a 24-item instrument used to measure the overall clinical symptom severity. The items cover symptoms of psychosis, depression, mania, anxiety and somatic concern. The instrument has been used previously in Ethiopia and has shown high internal consistency and reliability (11).

WHODAS (World Health Organization Disability Assessment Schedule), version 2.0: measures the level of difficulties individuals have over the previous 30 days due to a health condition.

The instrument covers 6 domains: understanding and communication, getting around, self-care, getting along with people, life activities and participation in society (12). The WHODAS 2.0 has been adapted for use in Ethiopia (13).

The Involvement Evaluation Questionnaire (IEQ): IEQ is a reliable and valid instrument, which assesses burden of caregiving on the basis of the perception of caregivers. It is an 81-item questionnaire to be completed by the caregivers of the patient. The Questionnaire has seven parts: a core section and six additional sections. The additional sections comprise questions about socio-demographics of the patient and the caregiver and contact variables; extra financial expenses; the General Health Questionnaire (GHQ-12), as measure of caregiver distress; professional help for the caregiver; consequences for patient's children; and one open question for additional remarks.

The core section of IEQ (27 items) assesses how often the caregiver experienced a burden in relation to caring during the previous 4 weeks. All items are scored on 5- point Likert scales (never, sometimes, regularly, often, and always). The items can be summarized as a total score or under the four domains: tension (9 items), supervision (6 items), worrying (6 items) and urging (8 items). Note that two items (items 29 and 43) are used in more than one domain. This means that the total score must be computed from the separate 27 items and not by just adding up the four subscales.

The domain "tension" refers to the interpersonal problem between patient and the caregiver; "urging" is the encouragement and motivation provided to the patient; "supervision" refers to the actual day to day care and guarding from danger; "worrying" refers to concerns related to patient's health and safety. Higher scores mean higher levels of caregiver burden. The instrument was translated and validated in several languages and used in different cultures such as in the EPSILON (European countries in European Psychiatric Services: Inputs Linked to Outcome domains and Needs) study involving five European countries (England, Netherlands, Spain, Italy and Denmark) (1,14) and several other countries (15-20).

The IEQ was translated into Amharic carefully through a consensus process by researchers with clinical and social science background and many years of experience in instrument translation and psychosocial research. The internal consistency and structure of the IEQ were also assessed. Although the IEQ is a self-administered questionnaire, in our case it was administered by trained and experienced lay data collectors. This was because most of the participants did not have adequate literacy to complete the IEQ.

Ethical approval

Ethical approval was obtained from the College of Health Sciences Institutional Review Board, Addis Ababa University (PSY/084/14). All families approached consented to participate.

Statistical analysis

The data were double entered using epidata version 3.1 and analyzed using the Statistical Package for Social Sciences (SPSS) version 12. We used a descriptive statistic for summarising the socio-demographics and the care profile of the study participants. We computed Cronbach's alpha values for internal consistency.

We run factor analysis and CFA in order to see the dimensions of the instrument. The 95% confidence intervals (CI) for the mean value were calculated whenever appropriate. We run bivariate and multivariate linear regression models to examine the association between IEQ total scores and patient and caregiver characteristics. We also used the mean scores of the total IEQ items and the domains for comparing the pattern of scores with some international data.

RESULTS

Participants and level of caregiver burden: Most caregivers were females (52.5%), married (67.6%), under 45 years of age (57.5%) and with little or no formal education (60.9%) (Table 1).

Caregivers were mainly first-degree relatives (84.7%)--children of the patients, spouses, siblings and parents--who lived in the same house with the patient (Table 2). Majority of cared for patients had schizophrenia spectrum disorder (85. 6%) with a small minority (14.7%) diagnosed with an affective psychosis.

Reliability of IEQ

The IEQ demonstrated relatively high internal consistency with Cronbach's alpha of 0.89 (for all the items). The four domains have also shown relatively high consistency (worrying=0.87, urging = 0.86, tension= 0.82 and supervision= 0.78). The factor analysis demonstrated that the 27 items load in to four factors, as in the original structure of the instrument and consistent with the above four domains (Worrying, urging, tension and supervision). Confirmatory factor analysis (CFA) showed that the total sum score of the IEQ can also be used on its own in addition to the four domains.

Table 1: Background characteristics of psychotic patients and their caregivers, Bui District, Ethiopia, December 2014 - July 2015.

Background Characteristics		Caregivers (n=299)		Patients (n=300)	
		Number	Percent	Number	Percent
Sex	Male	142	47.5	172	57.3
	Female	157	52. 5	128	42.7
	<25	46	15.4	65	21.7
Age	25-34	50	16.7	82	27.3
	35-44	76	25.4	79	26.3
	45-54	62	20.7	46	15.3
	55-64	46	15.4	15	5.0
	≥ 65	19	6.4	13	4.3
Marital Status	Single	50	16.7	136	45.3
	Married	202	67.6	111	37.0
	Divorced/ widowed	47	15.7	53	17.7
Religion	Christian	289	96.7	289	96.3
	Other	10	3.3	11	3.7
Ethnicity	Gurage	281	93.9	284	94.7
	Other	18	6.1	16	5.3
Education*	Illiterate	123	41.2	157	52.5
	Can read and write	59	19.7	53	17.7
	Formal education	117	39.1	89	29.8
	Agricultural work	108	36.24	76	25.5
Employment**	Self employed	41	13.76	16	5.37
	Housewife	93	31.21	58	19.5
	other employments	52	17.45	38	12.8
	Unemployed	4	1.34	110	36.9
Residence*	Urban	66	22.1	60	20.1
	Rural	233	77.9	239	79.9
Relative wealth	Very low and low	152	50.8	191	63.7
	Medium and above	147	49.2	109	36.3

Table 2: Profile of caregivers of patients with severe mental illness, Bui District, Ethiopia, December 2014 - July 2015

Care characteristic		Number	Percent
live in the same house with patient	No	51	17.1
	Yes	247	82.9
Relationship with patient	Parent	23	7.7
	Sibling	60	20.1
	Child	105	35.1
	Spouse	64	21.4
	Other family member	47	15.7
Lived together weeks	None	3	1.03
	Some days	40	13.7
	The full 4 weeks	251	85.4
Average time spent together	Less than 32 hours per week	64	21.4
	More than 32 hours per week	235	78.6

Caregiver burden and clinical and socio demographic correlates

The overall mean scores (95% Confidence Interval (CI) was 45.3 (43.2, 47.4) with mean domain scores of 15.5 for urging, 13.7 for worrying, 10.0 for supervision, and 9.7 for tension domains (Table 3).

Table 3: Caregivers' burden and mean Involvement Evaluation Questionnaire score by domain, Bui District, Ethiopia, December 2014 - July 2015 (n=299)

Burden domain	Mean	95% Confidence Interval	Range Min, max
Urging*	15.5	14.6, 16.4	0, 32
Supervision*	10.0	9.3, 10.7	0, 24
Tension**	9.7	8.9, 10.5	0, 36
Worrying**	13.7	12.9, 14.4	0, 24
Total IEQ score	45.3	43.2, 47.4	4, 107

Considering individual items of care involvement (Figure 1), encouraging patient to self-care (95%) and to eat (92%), and concern about the future of the patient (92%) were the most commonly endorsed burden items.

Concern about the general health of the patient, safety and managing finances without help from the care giver were endorsed by about four in five participants. Experience of burden of care was also endorsed by a similar proportion.

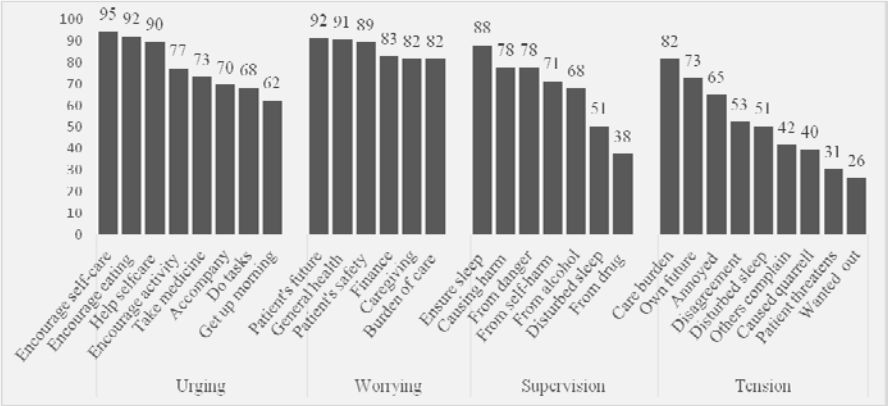

Figure 1: Percentage of caregivers endorsing individual items of the care sections of involvement, Bui District, Ethiopia, December 2014 - July 2015 (n=299)

In the unadjusted regression model (Table 4), sociodemographic characteristics of carers (female sex and being married), care characteristics (being first degree relative, living with patient and spending more than 32 hours per week with the patient), severity of illness in patient (high symptomatology and disability) as well as mental health of the carer (higher GHQ score) were associated with higher caregiver burden scores.

Formal education, employment status and higher relative wealth status were associated with lower caregiver burden scores. However, in the fully adjusted regression model (Table 4), only caregivers' sex (Adjusted mean difference=6.66; 95% CI=-0.01, 13.34; p=0.05), relationship with the patient across all first degree relatives compared with other relatives [Adjusted mean difference scores and p values for a parent caregiver 10.60, P< 0.01; child 8.82, P= 0.01; spouse 7.66, P< 0.02 and a sibling 8.53, P= 0.04)] were associated significantly with carer burden. High levels of symptomatology (Adjusted mean difference=0.16; 95% CI=0.03, 0.28; p=0.02) and disability (Adjusted mean difference=0.25; 95% CI=0.15, 0.34; p<0.01) in patient and high mental distress score in caregiver (Adjusted mean difference=0.45; 95% CI=0.13, 0.77; p=0.01) were also associated significantly with caregiver burden. The model explained 27.6% of the variance in caregivers' burden (Adj. r^2 = 27.64).

Table 4: Socio-demographic and clinical factors of caregivers associated with care burden, Bui District, Ethiopia, December 2014 - July 2015

	Caregiver characteristics	Crude mean Difference	95% Conf. Interval		Adjusted mean Difference	95% Conf. Interval		P value
Gender	Female	6.29	2.16	10.42	6.66	-0.01	13.34	0.05
Marital status	Married	10.07	4.46	15.68	2.64	-3.59	8.86	0.41
	Divorced/ Widowed	8.02	0.80	15.20	-0.64	-8.83	7.55	0.88
Education	Can read and write	0.73	-4.82	6.40	2.64	-2.62	7.89	0.32
	Formal education	-9.34	-13.86	-4.38	0.03	-5.35	5.41	0.99
Occupation	Agricultural work	-3.88	-8.93	1.16	3.62	-3.81	11.04	0.34
	Self employed	-3.61	-10.29	3.08	2.33	-3.85	8.50	0.46
	other employments	-10.69	-16.86	-4.52	-2.74	-9.20	3.72	0.41
	Unemployed	-14.79	-32.99	3.42	-4.20	-20.62	12.23	0.62
Live in the same house with patient	Yes	13.33	7.98	18.69	5.07	-0.62	10.77	0.08
Time spent together	More than 32 hours per week	6.76	1.72	11.81	2.16	-2.66	6.99	0.38
Relative wealth	medium and above	-8.38	-12.46	-4.30	-2.20	-6.20	1.80	0.28
Relationship with patient	Sibling	11.70	3.00	20.40	8.53	0.38	16.68	0.04
	Child	11.09	4.44	17.75	8.82	2.50	15.14	0.01
	Spouse	16.89	10.89	22.89	7.66	1.05	14.26	0.02
	Parent	18.63	12.07	25.20	10.60	3.46	17.73	<0.01
Total GHQ score		1.02	0.75	1.29	0.45	0.13	0.77	0.01
Patient clinical characteristics								
WHODAS Score		0.30	0.21	0.39	0.25	0.15	0.34	<0.01
Total BPRSE score		0.24	0.11	0.38	0.16	0.03	0.28	0.02

n=299 IEQ; Involvement evaluation questionnaire GHQ; General health questionnaire, WHODAS; World Health Organization disability assessment scale, BPRSE; Brief Psychiatric Rating Scale- Expanded version Note: References were: Male sex, Illiterate, house wife, single, not living in the same house, spent less than 32 hours per week and other family member

DISCUSSION

To our knowledge, this is the largest and detailed examination of the subjective dimensions of care giving in any African country or any LMIC. The IEQ, although being used for the first time in Ethiopia, it has good psychometric properties. Its internal consistency was comparable, even better, than the report by the developers (3). The Cronbach's α for worrying, urging, tension and supervision reported by the developers was respectively 0.80, 0.71, 0.85 and 0.77 compared with 0.87, 0.86, 0.82 and 0.78 in the Sodo sample. The identified domains and factor structure are also consistent. These findings suggest that the measurement of these care burden constructs in this study was adequately robust.

The study demonstrates the enormous and consistent toll of caregiving in this setting. The overall pattern of burden is either comparable or worse than what has been reported in diverse income group countries. In a study of the burden of involvement in care using the IEQ among care givers of patients with schizophrenia in five sites in five

European countries (Amestrdam-The Netherlands, London-United Kingdom, Santander-Spain, Copenhagen-Denmark, and Verona-Italy) (21), the crude mean score ranged from 14.28 in the Copenhagen carers to 29.61 among the Verona carers. In terms of domain specific scores, urging and worrying had the highest score.

The score for urging ranged from 4.68 in the Copenhagen carers to 8.72 among the Verona carers. For worrying, the score was lowest for Amesterdam (5.75) and highest for Santander (12.78). The score in the Sodo sample is also higher than reports from other countries—both developing and developed (16,18,19,22).

Although most domains and items of care were highly endorsed, the leading areas of involvement of caregivers were around encouragement of self-care, and concern regarding general health, safety and future of patient. Interpersonal aspects of care and conflict were less prominent and care givers rarely wanted to abandon the patient. While the relatively high burden is likely to be in part due to the very high treatment gap (23) and the virtual absence of statutory social care system, the extended family network may have mitigated the extreme impact of caregiving.

Three broad factors, related to caregiver characteristics, type of relationship and patient characteristics were associated with caregiver burden. Being a female caregiver and experience of mental distress by the caregiver were the two caregiver characteristics associated with high burden score. All first-degree relations had higher IEQ score. More severe illness symptomatology and disability in the patient were the patient characteristics associated with higher IEQ score. All these factors; female sex (24-29), being a first degree relative (6,20,29,30), more severe symptomatology and disability (6,25,28,30-33); have all been found to be associated with increased care burden. While the consistency of the findings speaks to the validity of the findings in this setting, it also speaks to the need for improving access to care to reduce symptoms of illness and disability and to the need of identifying interventions that support female caregivers in particular. There is also scope for mobilizing the rich community resources and networks (23).

The findings of this study should be interpreted in the context of certain limitations. The study was cross-sectional, and direction of causality cannot be ascertained. Patients had no single diagnosis although over 80% of the sample had a diagnosis of schizophrenia spectrum disorder. However, in the context of primary care, which this study was focused on, a broad diagnosis is more appropriate. On the other hand, the population-based recruitment, the focus on primary care or integrated care, the relatively large sample size and the use of an instrument with robust characteristics make the findings meaningful, relevant and of interest.

Conclusion

In conclusion, the findings of the present study indicated that caregivers of persons with severe mental illness experience an elevated level of burden, particularly related to encouraging the patient and worrying about the patient. While caregivers in this study bear their 'burden' with little complaint, as shown in the low level of interpersonal tension with the patient, improving care provision to improve symptoms and disability in patients and mobilization of broader support should be considered urgent priority.

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Competing interest

The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

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ORIGINAL ARTICLE

PREVALENCE AND DETERMINANTS OF FATIGUE AMONG PARKINSON'S DISEASE PATIENTS IN ETHIOPIA

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ABSTRACT

Introduction: *Fatigue is a severe problem for many people living with Parkinson's disease. Best estimates suggest that more than 50% of patients with Parkinson's disease experience this debilitating symptom. Fatigue is related to excessive daytime sleepiness and in certain studies with disease progression. There has been no prior report on Fatigue among patients with Parkinson's disease living in Ethiopia.*

Objective: *The present study is aimed at assessing the prevalence and determinant of fatigue among patients with Parkinson's disease in Ethiopia.*

Methods: *A cross-sectional study of all Parkinson's disease patients attending the follow-up clinics of the Departments of Neurology at Tikur Anbessa and Zewditu Memorial Hospital in Addis Ababa, Ethiopia, from July 1 to October 30, 2015 was conducted. We collected information using a structured questionnaire which assessed demographic information, clinical history, the Parkinson's fatigue scale item sixteen (distressing fatigue defined as mean score ≥3.3) and the Epworth Sleepiness Scale.*

Results: *Of the 155 patients surveyed, 155 patients responded for PFS-16 items with mean (±SD) score of 3.88 (±0.79). Distressing fatigue was noted on 120 (79.5%) of the respondents. Excessive day time sleepiness according to the Epworth Sleep Scale ≥10 (OR 3.39; 95% CI 1.41 - 8.20, P=0.004) and unemployment (OR 2.71; 95% CI 1.19 – 6.17, P=0.016) associated with distressing fatigue. There was no statistical association with age, gender, Parkinson's disease stage, duration of Parkinson's disease symptoms, previous history of sleep disturbance, Levodopa or Trihexyphenidyl use and higher Parkinson's disease Sleep Scale version two score.*

Conclusions: *The prevalence of distressing fatigue in Ethiopian patients with Parkinson's disease is substantially high. Further investigations into contributors in our patients with Parkinson's disease are needed.*

Keywords: *Parkinson's disease, Fatigue, Ethiopia*

BACKGROUND

Parkinson's disease (PD) is a neurodegenerative disorder associated with a loss of dopamine-producing neurons in the substantia nigra pars compacta. The disease was described by James Parkinson in 1817, and his description remains remarkably accurate (1). It is characterized by abnormal motor symptoms such as bradykinesia, tremor, rigidity, and postural instability (2). However, the non-motor symptoms (NMS) of PD, including fatigue, cognitive impairment, depression, sleep disorders, and autonomic dysfunction are also equally important (3).

Since Fatigue is a subjective feeling, with no biological markers, it is difficult to describe and its definition is influenced by the background and culture of the patient (4). Subtypes of fatigues are peripheral fatigue and mental fatigue. Fatigue is a common problem for the general population and is particularly challenging for people with Parkinson's disease (PD) (5).

Available estimates suggest that more than 50% of patients' experience this debilitating symptom. Fatigue has been described to be the most troublesome aspect of PD in about one-third of patients, yet it is poorly understood. Fatigue could be present before, at the time of diagnosis of PD in untreated patients or during the course of the disease (4).

A cross-sectional study conducted in Italian patients reveled 33.8% reported Distressing fatigue (PFS-16 mean score ≥3.3) [6]. Patients with distressing fatigue were older (P=0.044) and had a longer duration of PD (P< 0.0001) than those without distressing fatigue (6).

The presence of distressing fatigue was associated with higher total Unified Parkinson's Disease Rating Scale (UPDRS) scores, poorer quality of life, worse social and psychological behaviors.

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There have been limited recent studies published on PD in sub Saharan Africa (7-14) and far fewer from Ethiopia (15-21) and no published data on fatigue in people with PD living in Ethiopia. This study is aimed at filling this knowledge gap by assessing the prevalence of fatigue and their determinant factors in people living with PD in Ethiopia.

METHODS

Addis Ababa University is the only training center for neurologists in Ethiopia. Its main hospitals include the Tikur Anbessa and Zewditu Memorial hospitals. A cross-sectional survey was conducted from July 1, 2015 to October 30, 2015 in the two referral hospitals. All patients diagnosed with PD attending the neurology clinics in these hospitals during the study period were the source population. Patients were included if they were ≥18 years old, fulfilled the UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria for the diagnosis of PD, and gave informed verbal consent for study participation.

The diagnostic criteria consisted of three major entirely clinical components: Diagnosis of Parkinsonian Syndrome, exclusion criteria for Parkinson's disease and supportive prospective positive criteria for Parkinson's disease (22). Patients were excluded if they had Parkinsonism due to other causes (like drug induced Parkinsonism, vascular Parkinsonism, Parkinson plus syndrome which were based on UK Parkinson's Disease Society Brain Bank Clinical Diagnostic Criteria for the diagnosis) or if they refused consent. Clinical data was collected using a structured questionnaire in English and Amharic which assessed demographic data, a detailed clinical history including symptoms and duration of PD, medication history and neurologic examination. We used two data collection instruments: the Parkinson Fatigue Scale 16 item (PFS-16), (23)] and the Epworth Sleepiness Scale (ESS) questionnaires (24, 25).

The PFS-16 is a scale addressing 16 commonly reported symptoms associated with Fatigue. The presence of Fatigue was evaluated using PFS-16 which consists of 16 items. Each item was rated on a scale from 1-5 one is for strongly disagree and 5 being strongly agree. The PFS-16 scale was designed to tap a single construct encompassing the physical aspects fatigue and their impact on the patient's daily function (26). The scale deliberately excludes emotional and cognitive features that may occur as part of the fatigue experience, but which may also occur independently in Parkinsonism. The scale has good intrinsic properties and satisfactory test-retest reliability. It shows reasonable associations with other measures of fatigue and can identify patients who self-report the presence of fatigue, and particularly those in whom fatigue is a problem. Cut-off scores are provided in both cases with good specificity and sensitivity (26). The scale was also validated in different country (27, 28).

The ESS is used as a subjective measure of a patient's daytime sleepiness. This scale has a list of eight situations in which patients rate their likelihood of becoming sleepy on a scale of 0-3. Total score ranges from 0 to 24. A score of 10-15 suggests possible excessive daytime somnolence, and a score of 16-24 suggests definite excessive daytime somnolence (24, 25)**.** Unfortunately, we didn't perform formal reliability/validity study considering the setup we are in, but the PFS-16 and ESS were translated from English into Amharic and pilot-tested on 10 subjects. These subjects were not included in the study results.

Findings from the pre-test were used to modify questions on the standard questionnaire. The slight amendments were done on ESS up on translation to Amharic version by using similar scenarios considering that some of our patients were not having television and car.

Analysis was performed using SPSS/PC version 20.0 software packages for statistical analysis (SPSS). Descriptive summaries were employed to describe socio-demographic and clinical characteristics. Appropriate measures of central tendency, frequency distribution, cross tabulation, Fisher's Exact test and binary logistic regression analysis were used in the analysis. Odds ratios with 95% confidence intervals were calculated to describe the strength of the association between the outcome and key determinant factors. A P-value ≤0.05 was considered a statistically significant association.

Protocol approvals were obtained from the ethical review Committee of the Department of Neurology and the Institutional Review Board and Research and Publication Committee of the College of Health Sciences of Addis Ababa University. Verbal informed patient consent was obtained before study enrollment. Patients were informed participation was on voluntary basis, and they had the right to withdraw from the study at any point without any consequences. Patient data was deidentified during subsequent analysis and dissemination.

RESULTS

A total of 151 study participants were recruited in this study: 124 (82.1%) male and 27 (17.9%) female. Table 1 shows the demographics of our participants. The mean duration of symptoms, duration since PD diagnosis and duration of PD treatment were 6.37, 4.90, and 4.68 years, respectively. All patients were taking levodopa while 24.5% were taking trihexyphenidyl in addition to levodopa and 7.3% patients were taking medications for hypertension and diabetes mellitus. No patient was taking other anti-parkinsonian agents (e.g. dopamine agonist, amantadine) or was on any other medications other than mentioned.

Presences of comorbidities were also assessed. Of the study participants only 11 patients were having medical comorbidities; five patients had diabetes mellitus and six had hypertension.

Table 1: Socio-demographic characteristics of patients with Parkinson's disease, Tikur Anbessa and Zewditu Memorial hospitals, Addis Ababa. July 1, 2015 to October 30, 2015.

Variables	Number (%)
Gender	
Female	27 (17.9)
Male	124 (82.1)
Age	
<60 years	70 (46.4)
≥60 years	81 (53.6)
Marital status	
Never married	6 (3.9)
Married	117 (77.6)
Widowed	19 (12.6)
Separated/divorced	9 (5.9)
Duration of PD symptom in years	
<5 years	63 (41.7)
≥5 years	88 (58.3)
Employment status	
Employed	42 (27.8)
Unemployed	109 (72.2)
Educational status	
No formal education	48 (31.8)
Primary education	44 (29.2)
Secondary education	35 (23.2)
More than secondary education	24 (15.8)
Hoehn and Yahr Stage	
Stage 1	36 (23.8)
Stage 2	46 (30.5)
Stage 3	41 (27.2)
Stage 4	23 (15.2)
Stage 5	5 (3.3)
Previous history of sleep disorder	
Yes	37 (23.9)
No	118 (76.1)
Trihexyphenidyl use	
Yes	37 (24.5)
No	114 (75.5)
Levodopa use	151 (100)

Table 2 shows the results of the PFS-16 scores with independent variables. Over a three fourth 120 (79.5%) of patients were having distressing Fatigue (Defined as PFS-16 Mean score ≥3.3) mean score (±SD) being 3.88 (±0.79). On univariate analysis, there was a statistically significant association between distressing fatigue and excessive day time sleepiness, ESS ≥ 10 (OR 3.39; 95% CI 1.41 - 8.20, P=0.004) and unemployment (OR 2.71; 95% CI 1.19 – 6.17P p=0.016). On univariate analysis there was no statistical association with age, gender, Hoehn & Yahr stage, duration of PD symptoms, and presence of hypertension or diabetes mellitus, previous history of sleep disturbance, levodopa or trihexyphenidyl use, marital and educational status.

Table 2: Results of Parkinson Disease Fatigue scale item 16 with independent variables of the study participants, Tikur Anbessa and Zewditu Memorial hospitals, Addis Ababa. July 1, 2015 to October 30, 2015.

	PFS-16 mean score		**OR (95% CI)**	**P-value**
	<3.3	**≥3.3**		
ESS total score				
<10	23	55	3.39 (1.41 - 8.20)	0.004
≥10	8	65		
Employment status				
Employed	14	28	2.70 (1.19 – 6.17)	0.016
Unemployed	17	92		
Age				
<60yrs	17	53	1.54 (0.69 – 3.39)	0.195
≥60yrs	14	67		
Sex				
Male	29	95	0.26 (0.06 - 1.17)	0.047
Female	2	25		
PD stage				
Hoehn & Yahr stage <3	19	63	1.43 (0.64 – 3.21)	0.251
Hoehn & Yahr stage ≥3	12	57		
Previous history of sleep disorder				
Yes	9	27	1.39 (0.58 – 3.38)	0.302
No	12	92		
Trihexyphenidyl use				
Yes	11	26	0.50 (0.21 – 1.18)	0.080
No	20	94		
Duration of PD symptom				
<5Years	17	46	1.95 (0.88 – 4.34)	0.073
≥5 Years	14	74		
Marital Status				
Have partner living with	27	90	2.25 (0.73 – 6.95)	0.113
No partner	4	30		

A logistic regression analysis was performed to determine factors associated with a fatigue. On logistic regression there was no statistical association with age, gender, Hoehn & Yahr stage, excessive day time sleepiness, unemployment, duration of PD symptoms, and previous history of sleep disturbance, levodopa or trihexyphenidyl use, marital and educational status.

DISCUSSION

The present study revealed that Ethiopian PD patients exhibit one of the highest prevalence of distressing Fatigue with more than three out of four patients reporting the problem (79.5%). This is substantially higher compared to estimates from countries such as Fatigue reported in 42.4% of Chinese (29), 57.9% of Polish (30) and 34% of Norwegian PD patients (31).

A study done on Italian PD patients using PFS-16 reported 33.80% of patients were having distressing fatigue (PFS-16 mean score ≥3.3) (6) which was much lower than our finding. This could be due to disparity in cultural and economic status of the population (4). In PD patients, the wide range of prevalence of fatigue (37–56%) is largely because of varying definitions of fatigue and populations tested (32). This difference could be due to the presence of diverse tools to asses fatigue in PD patients and its definition.

A study done on Slovakian PD patients using multidimensional fatigue inventory (MFI) showed that out of 119 PD patients (78.8% of the sample) were fatigued in at least one of MFI domain (33). This is nearly comparable with our finding. Our study revealed that distressing fatigue was associated with Excessive day time sleepiness (P=0.004), which was also shown on other study that the severity of fatigue was positively associated with excessive daytime sleepiness (p = 0.009) (29).

On our study 7.3% of the patients were having Hypertension and Diabetes Mellitus. However, the presence of these disease entities didn't show statistically significant association with the presence of distressing fatigue; this finding was also reported on Italian PD patients (6).

In contrary to our study finding, a cross-sectional study conducted on Italian PD patients reveled that patients with distressing fatigue were older (p =0.044) and had a longer duration of PD (P< 0.0001) than those without distressing fatigue (6). This could be due to longer mean duration of PD symptom and higher mean age of the study participants of the Italian PD patients. Our study also discovered that unemployment is associated with distressing fatigue (P=0.016) which was not reveled in other studies.

Our study had several limitations. One significant limitation of our study was the data were obtained from only two teaching hospitals in Ethiopia which may not fully representative of the overall PD patients in the country and the sample consisted predominantly of male patients.

The other significant limitation of our study was our inability to assess psycho-behavioral factors that contribute for fatigue like depression and anxiety. One study revealed that the presence of distressing fatigue was associated with worse psychological behaviors and a higher severity of depressive symptoms (p < 0.001) (6).

Conclusions: The prevalence of distressing fatigue in Ethiopian PD patient is among the highest compared to earlier reports from several countries. Further studies need to focus on substantiating the current high prevalence and investigate contributing factors to better understand the extent and distribution of distressing fatigue in low income setting.

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Competing interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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ORIGINAL ARTICLE

PREVALENCE OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE AMONG PATIENTS SUCCESSFULLY TREATED FOR PULMONARY TUBERCULOSIS

Amsalu Bekele, MD[1*], Meron Getachew, MPH[2], Charles B. Sherman, MD,MPH[3], Neil W. Schluger, MD[4]

ABSTRACT

Introduction: *Chronic Obstructive Pulmonary Disease is currently the fourth leading cause of death in the world. In 2012, more than 3 million people died of Chronic Obstructive Pulmonary Disease, accounting for 6% of all deaths globally. Several epidemiologic studies have shown that pulmonary tuberculosis is emerging as a potential risk factor in the pathogenesis and severity of Chronic Obstructive Pulmonary Disease. This finding is especially concerning given the high prevalence of pulmonary tuberculosis in low resource countries.*

Objective: *This study was conducted to evaluate the prevalence of Chronic Obstructive Pulmonary Disease in patients successfully treated (cured plus treatment completed) for pulmonary tuberculosis seen at Tikur Anbessa Specialized Hospital, the largest public tertiary hospital in Ethiopia.*

Methodology: *We conducted a cross-sectional study of patients > 15 years of age who were successfully treated for pulmonary tuberculosis and followed in the Chest Unit at Tikur Anbessa Specialized Hospital between August 2016 to September 2017. Patients with signs and symptoms of active pulmonary tuberculosis were excluded. All patients had lung function measured using a Diagnostic EasyOne Plus model 2001 SN spirometer. Spirometric acceptability and reproducibility were determined using the published criteria of the European Respiratory Society/American Thoracic Society. A diagnosis of Chronic Obstructive Pulmonary Disease was based on a post-bronchodilator FEV1/FVC<70% as recommended by the Chronic Obstructive Pulmonary Disease guidelines.*

Results: *A total of 99 patients were included in the analysis. Of these 55(55.6%) were male; the mean age of the group was 42.7 years. Forty-one of 99 (41.4%) study participants had post-bronchodilator FEV1/FVC<70%, meeting the study criteria for Chronic Obstructive Pulmonary Disease. This percent was approximately 8 times higher than the 5% previously determined for Chronic Obstructive Pulmonary Disease in the general population for sub Saharan Africa. In addition, a majority of those diagnosed with Chronic Obstructive Pulmonary Disease in our study had moderate to severe Chronic Obstructive Pulmonary Disease stage disease.*

Conclusions: *The prevalence of Chronic Obstructive Pulmonary Disease is high in our Ethiopian patients who were successfully treated for pulmonary tuberculosis , and higher than expected from previously published population based studies. Although selection bias may have contributed to our results, we believe that patients successfully treated for pulmonary tuberculosis are at significant risk for developing Chronic Obstructive Pulmonary Disease, and should be strongly considered for screening and possible treatment.*

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive life-threatening lung disease that causes breathlessness (initially with exertion) and predisposes to exacerbations and serious illness (1). In 2016, the Global Burden of Disease Study reported a global COPD prevalence of 251 million cases.

Furthermore, in 2012, there were an estimated 3.17 million deaths from COPD, accounting for 5% of all deaths globally that year. More than 90% of COPD deaths occur in low- and middle- income countries (2).

COPD is characterized by chronic airway inflammation with progressive lung function deterioration and is a major cause of not only mortality but also morbidity and disability (3). There is growing evidence of co-morbidity between COPD and tuberculosis (TB), the leading global cause of death due to respiratory infection (3). Tuberculosis poses a global public health threat and remains the leading cause of death among infectious diseases, especially in low- and middle-income countries(4). While TB can occur in any organ or tissue, the respiratory system is the most common site of active disease. Without treatment, PTB has a mortality rate of 50% within five years (5).

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Although standard anti-TB treatment is highly effective, with a rapid resolution of symptoms and low rate of relapse, non-adherence remains a great obstacle to successful treatment (6). Even after completing treatment for PTB, approximately two-thirds of patients have pulmonary function abnormalities, with an obstructive defect being the main abnormality detected (7-10).Those previously treated PTB patients have a greater risk of death from respiratory causes (11-14) and are thought to be significant contributors to the growing worldwide burden of COPD (15-18).

In Ethiopia, a low resource country with a high burden of TB, the prevalence of COPD among those previously treated for PTB is unknown. The main objective of this study was to determine the prevalence of COPD among patients previously treated for PTB who had regular follow up in the Chest Unit of Tikur Anbessa Specialized Hospital (TASH).

PATIENTS AND METHODS

Study design and population

We conducted a hospital-based descriptive cross-sectional study in the Chest Unit of TASH from August 2016 to September 2017. TASH is tertiary level hospital in Addis Ababa, Ethiopia, offering diagnosis and treatment for approximately 370,000–400,000 patients per year. There are 16 outpatient clinics located within the hospital; the Chest Unit itself has over 500 visits/month for patients with various respiratory symptoms and pulmonary diseases including previously treated PTB. It was an optimal site for the study because of the large volume of patients, the well-organized longitudinal database, and the availability of diagnostic expertise with spirometry, bronchoscopy, Gene Xpert, and chest imaging.

The study population included all consecutive Chest Unit patients who were aged $\geq$15 years who had previously been successfully treated (cured or treatment completed) for PTB. Patients with active TB were excluded from the study using WHO systematic screening criteria. Data were collected from clinical records and patient interviews using a structured questionnaire. Information obtained included socio-demographics, PTB diagnosis and treatment history, smoking history, and exposure to biomass fuel from domestic cooking.

All participants provided written informed consent. Ethical approval for the study was obtained from the College of Health Sciences, Addis Ababa University Institutional Review Board.

Pulmonary function measurements

Lung function was measured for all patients using a Diagnostic EasyOne Plus model 2001 SN spirometer by an appropriately-trained technician. Spirometric acceptability and reproducibility were determined using the published criteria of the European Respiratory Society and the American Thoracic Society (19).

Based on the spirometric findings, patients were first classified as normal or abnormal (i.e., obstructive, restrictive, mixed) according to the algorithm from the National Lung Health Education Program (NLHEP) (20).Airflow obstruction was defined as an FEV_1/FVC ratio below the lower limit of normal (LLN) and FVC above LLN. Restriction was defined as an FEV_1/FVC ratio$\geq$ LLN and an FVC < LLN. A mixed pattern was defined as a FEV_1/FVC ratio, FEV_1, and FVC all < LLN. For those with airflow obstruction, a diagnosis of COPD was based on a post-bronchodilator FEV1/FVC<70% as recommended by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines (21). Severity of obstruction (mild, moderate, and severe) was classified according to the GOLD guidelines (21) and the American Thoracic Society/European Respiratory Society (ATS/ ERS) task force recommendations (19), respectively.

Subjects whose spirometric tests did not meet ATS/ ERS acceptability and reproducibility criteria and those with significant post-bronchodilator reversibility of more than 12% were excluded (19).

Data analysis

Data were analyzed using SPSS (version 20.0) statistical software. Means ± standard deviation (SD) and proportions were calculated for continuous and categorical data respectively. Median and interquartile range (IQR) was used for non-normally distributed numerical data. We assumed that the FEV_1, FVC, FEV_1/FVC ratio data were normally distributed.

Linear regression was used for continuous variables (FEV_1, FVC, FEV_1/FVC,) and logistic regression was employed to determine predictors of COPD; the dependent variable was COPD (present or absent), and the independent variables included age, gender, level of education, smoking status, TB episode number (first episode or recurrent), HIV sero-status (positive or negative) and biomass exposure. Findings were considered statistically significant if $p<0.05$.

RESULTS

A total of 99 patients were included in the analysis. There was a male–female ratio of 55:44 (56%:44%) and a mean age for the group of 42.7 years. Thirty-five (35.4%) of the subjects were in the 31–45 years age group. Forty-six (46.5 %) had exposure to biomass, of which 31(31.3%) had ≥10-years exposure.

A history of active smoking and second hand smoke exposure were noted in 16(16.2%) and 7 (7.1%) patients, respectively. The median smoking pack year was 5.5 with IQR (3-17.5). Most of the patients, 68 (68.7%), had a history of one episode of PTB, while 31(31.3 %) had two or more episodes of PTB. Approximately 7.1 % of the group was HIV co-infected, 28.3% were HIV negative, and 64.6 % had an unknown HIV sero-status. (Table 1)

Table 1: Socio-demographic characteristics of pulmonary tuberculosis patients at the Chest Clinic, Tikur Anbessa Specialized Hospital, August 2016-September 2017 (N=99)

Characteristics	Frequency	Percent (%)
Age groups (years)		
15-30	24	24.2
31-45	35	35.4
46-60	32	32.3
≥65	8	8.1
Sex		
Male	55	55.6
Female	44	44.4
Level of education		
Illiterate	37	37.4
Literate	62	62.6
Occupation		
Unemployed	16	16.2
Employed	55	55.6
Farming	12	12.1
Housewife	16	16.2
Smoking history		
Never smoked	83	83.8
Smoker (in the past or still smoking)	16	16.2
Passive smoker		
Yes	7	7.1
No	92	92.9
TB episode		
1X	68	68.7
≥2X	31	31.3
HIV Status		
Positive	7	7.1
Negative	28	28.3
Unknown	64	64.6
History of Asthma		
Yes	16	16.2
No	83	83.8
Cooking History ≥10years (Biomass fuel)		
Yes	46	46.5
No	53	53.5

The group's mean spirometric values were: FEV_1 53.9 % predicted, FVC 63.1% predicted, and FEV_1/ FVC 59.2%. Of the participants 14(14.1%) had normal spirometry, 41(41.1%) had obstructive spirometry, 42(42.4%) had restrictive spirometry, and 2(2.0%) had a mixed pattern. (Table 2)

Table 2: Types of lung function abnormalities in pulmonary tuberculosis patients, Chest Clinic, Tikur Anbessa Specialized Hospital, August 2016- September 2017 (N=99)

No	Type of Impairment	Number (%)
1	Normal	14 (14.1)
2	Obstructive pattern (FEV1/FVC ratio < LLN	41(41.4)
3	Restrictive pattern (FEV1/FVC ratio >LLN	42(42.2)
4	Mixed pattern (FEV1/FVC ratio <LLN	2(2.0)

In our study 14(14.1%) were normal, 41(41.4%) had an obstructive pattern, 42(42.4%) had a restrictive pattern and 2(2%) had a mixed pattern (Table 2). Forty-one of 99(41.4%) study participants met the criteria for COPD with a post-bronchodilator FEV_1/ FVC<70%. In addition, most of those participants diagnosed with COPD had GOLD stage II (moderate disease) which was detected in 18(43.9%) patients. Fourteen (34.1%) and 7(17.1%) of patients were diagnosed with stage III (severe) or stage IV (very severe) disease stage respectively (Figure 1). No additional risk factors were identified for those post-PTB subjects with spirometric findings of COPD.

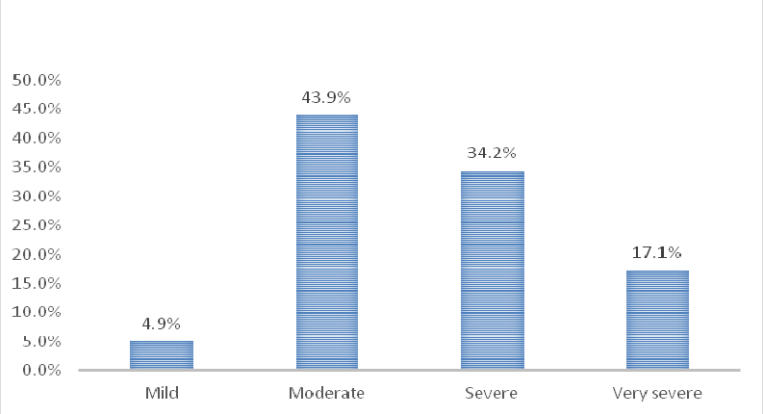

Figure 1: Severity of Chronic Obstructive Lung Disease in pulmonary tuberculosis patients, Chest Clinic, Tikur Anbessa Specialized Hospital (N=41)

DISCUSSION

In our study, 41 (41.2%) successfully treated PTB patients followed in the Chest Unit of TASH fulfilled the spirometric criteria of COPD. Furthermore, most of these patients had moderate and severe stage disease.

These findings suggest that successfully treated PTB can be a significant risk factor for reduced lung function, and may be a cause of chronic lung disease, especially in countries where the tuberculosis burden is high, and diagnosis and treatment may be delayed.

Our results are similar to other previously published research. A large multicenter population-based study (N=5,571 participants) performed in 5 Latin American countries, PLATINO, found that FEV_1 was reduced compared to FVC in most of those with physician diagnosed PTB (17). Another study done in Pakistan reported 26(55.3%) post-PTB subjects had an obstructive ventilatory defect, of which 18(69.2%) had severe COPD impairment (22). In their study, Wilcox and Ferguson determined that 65% of those patients previously treated for PTB more than 10 years earlier showed an obstructive ventilatory defect (23). Additionally, the obstructive changes correlated with the degree of residual scarring on chest radiograph.

A study conducted in Egypt on chronic obstructive pulmonary disease in treated pulmonary tuberculous patients demonstrated irreversible obstructive pattern in 22(44%) patients who underwent pulmonary function testing, denoting chronic obstructive pulmonary disease (COPD). Seven patients had a restrictive ventilatory defect, and three patients had a mixed obstructive and restrictive pattern.

In the same study, 11(50%) patients had mild obstruction, 9(40.9%) patients had moderate obstruction, and two (9.1%) patients had severe obstruction (24). Our results may have differed slightly from those of others as our patients were younger, had their PTB successfully treated, and were followed in an outpatient setting of a large tertiary referral center.

Although in high income countries, tobacco smoking is recognized as an important risk factor of COPD, the prevalence of COPD among non-smokers in those countries is estimated to be 6.6% of the population with an estimated 25-45% of COPD patients having never smoked (25,26). Indoor air pollution from biomass fuel, occupational dusts, and exposure to toxic gases, a history of pulmonary tuberculosis (PTB), chronic asthma, poor socio-economic status, and genetic factors are also recognized as potential factors contributing to the diagnosis of COPD (25,27).

A nationwide survey conducted in South Africa suggests that in a TB endemic area, pulmonary TB may be the strongest risk factor of COPD (28). We were unable to determine additional risk factors for COPD in our post-TB patients, possibly reflecting the data collected and the relatively small number of participants.

Limitations

There were several study limitations. Our sample size was relatively small, lowering the likelihood of finding all the significant associations. This was especially evident in determining risk factors for COPD other than previous PTB. The study was conducted at a tertiary referral center raising the possibility of selection bias. Finally, the study was conducted at a single center, whereas a multicenter study could have produced results that would have been more robust.

Conclusion

The prevalence of COPD was high in our Ethiopian patients who were successfully treated for PTB, and higher than expected from previously published population based studies.

Although selection bias may have contributed to our results, we believe that patients successfully treated for PTB are at significant risk for developing COPD, and should be strongly considered for screening and possible treatment.

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Competing interest

The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

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ORIGINAL ARTICLE

CLINICAL PROFILE OF ETHIOPIAN PATIENTS WITH RHEGMATOGENOUS RETINAL DETACHMENT

Sadik Taju Shrief , MD[1*], Tiliksew Teshome Tessema, MD[1], Sintayehu Desta Delelegn, MD[1]

ABSTRACT

Introduction*: Clinical presentation of rhegmatogenous retinal detachment in the developing world is not very well known.*

Objective: *This study reports the clinical presentation of 321 cases of rhegmatogenous retinal detachments in Ethiopian patients.*

Methods: *A prospective cross-sectional descriptive study was undertaken to evaluate the clinical presentation of all patients with rhegmatogenous retinal detachment seen at the retina clinic of Menelik II Hospital from October 2013 to February 2016. Complete ophthalmic examination was done including ultrasound when the media was hazy.*

Results: *The mean age at presentation was 41.8 years with male to female ratio of 2.3:1. Two hundred eighty of the involved eyes (87.2%) were blind (visual acuity < 3/60). The duration of symptoms was over 1 month in 220 (68.5%) cases and in 268 ((83.5%) the macula was detached at presentation. Long distance from the tertiary center was the main reason number (25.8%) for late presentation. Myopia observed in 151(47%) cases, was the major predisposing factor.*

Conclusions: *The profile of rhegmatogenous retinal detachment among Ethiopians presenting at a tertiary care center includes many young cases, late presentations and macula-off detachments, commonly related to myopia. Improvements in primary health care and education should reduce the delay in presentation.*

Key words: *rhegmatogenous retinal detachment, myopia, late presentation.*

INTRODUCTION

Retinal diseases are traditionally given low priority in the developing world because of the overwhelming burden of blindness and low vision caused by diseases like cataract and trachoma. Leading causes of blindness and low vision in the developed world such as age-related macular degeneration and diabetic retinopathy were believed to have low prevalence in the developing world especially Africa. There are changing trends in the prevalence of retinal diseases in the developing world. With changing lifestyles and demographics in the developing world, retinal diseases are assuming an important role in causing blindness and low vision. (1). A population-based study conducted in an urban area in India found that the top 3 causes of blindness were cataract (29.7%), retinal disease (12.5%), and corneal disease (15.4%) (2).

Rhegmatogenous retinal detachment (RRD) is one of the major retinal disorders which leads to unilateral or bilateral blindness if untreated. RRD in the developing world differs from RRD in the developed world. These differences may arise because of genetic differences or geographic and socio-economic factors (3). There are few data about the incidence of RRD and its clinical features in the developing world especially from Africa. The purpose of this study was to determine the characteristics of RRD at a tertiary eye care center in Addis Ababa, Ethiopia.

PATIENTS AND METHODS

A prospective cross-sectional study was conducted on all consecutive patients with RRD seen at the Retina Clinic of Menelik II Hospital from October 2013 to February 2016. The eye department at Menelik II Hospital is the largest eye department in the country and provides a referral service to patients coming from all over the country.

Demographic data including age and sex were recorded. In the history, the presenting complaint and duration of the complaint were recorded. Past ocular history including history of trauma and ocular surgery were sought and recorded. Information about the time and place where the patients were first seen,

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and about the health institutions involved in referral of the patients to Menelik II Hospital was documented. For patients with duration of detachment longer than one week, reasons for late presentation were elicited.

Best corrected visual acuity was taken, and the presence of myopia was sought and recorded. Comprehensive eye examination was carried out paying attention to presence of corneal opacity, posterior synechae and lenticular status including cataract, aphakia and pseudophakia. Dilated fundus examination was done with non-contact slit lamp biomicroscopy using a 90D lens and indirect ophthalmoscopy. The presence of vitreous pathologies including vitreous pigment/cells and hemorrhage were noted. The extent of retinal detachment in the four quadrants, macular status, the number, type and location of breaks were documented. B-scan ultrasonography (Sonomed) was performed for patients precluding clear view of the posterior segment. The initial evaluations were done by residents at the retina clinic. Consultant Ophthalmologists confirmed the findings and set the treatment plan.

One RRD in one eye was considered as a case. If a patient presented with simultaneous bilateral RRD, this was regarded as one case. If the fellow eye had developed RRD within the study period, this was re-

Data were entered onto SPSS version 15.0 and appropriate statistics were computed between baseline characteristics of patients with a pattern of retinal detachment using Fisher Exact test. P-values below 0.05 were considered statistically significant.

Ethical clearance to conduct the study was obtained from the Research and Publication Committee of the Department of Ophthalmology, Medical Faculty Addis Ababa University. Similarly, verbal consent was obtained from each participant and subjects had the right to withdraw from the study at any time.

RESULTS

A total of 321 incident cases of rhegmatogenous retinal detachment who were seen at Menelik II Hospital during the study period were included. The sociodemographic and baseline characteristics of the patients are shown in Table 1. There were 224 (69.8%) men and 97 (30.2%) women with a male to female ratio of 2.3:1. The mean age at presentation was 41.8 years ± SD 16.6 (range: 9-76 years, median: 40 years). Fifty-eight (18.1%) patients were illiterate and 149 (46.4%) cases were from outside of Addis Ababa.

Table 1: Sociodemographic and baseline characteristics of Rhegmatogenous Retinal Detachment Cases seen at Menelik II Hospital, Addis Ababa, Ethiopia, October 2013-February 2016. (N=321)

	Sex		
	Male (N)	**Female (N)**	**Total N (%)**
Age (years)			
0-9	1	0	1 (0.32)
10-19	21	6	27 (8.4)
20-29	37	19	56(17.4)
30-39	43	23	66 (20.6)
40-49	41	15	56 (17.4)
50-59	39	17	56 (17.4)
60-69	32	11	43 (13.4)
>70	10	6	16 (5.0)
Educational level			
Illiterate	30	28	60 (18.7)
Read and write	61	29	87 (27.1)
Grade 1-6	62	21	81 (25.2)
Grade 7-12	56	17	75 (22.4)
Grade 12 and above	15	2	18 (5.6)
Risk factors			
Myopia	100	51	151 (47.0)
Trauma	71	30	101 (31.5
Cataract surgery	39	13	52 (16.2)
Others	14	3	17 (5. 3
Total	224	97	321

Reduction of central vision was the presenting compliant in almost all the patients write number(97.5%). The mean duration after the onset of symptom was 26 (± 40.3) weeks. Only 18(5.6%) patients presented within one week after the onset of symptoms. Those who presented within four weeks accounted for 101 (31.4%) whereas 71 (22.1%) presented six months after the onset of their complaint (Table 2). Only 8 (2.5%) patients directly visited the tertiary eye care center, the rest were referred from other clinics and secondary eye care units. The common reasons for late presentation given by the study subjects with duration of complaint exceeding one week was the long distance from the tertiary eye care center 83 (25.9%) followed by late referral from primary and secondary eye care centers 79 (24.6%) and long appointment for evaluation even at the referral hospital 73 (22.7%). Surprisingly, among patients with late referral 208 (64.7%) were from Addis Ababa, a city where the referral center is located (Table 2). Two hundred eighty cases (87.2%) had visual acuity in the range of blindness (< 3/60). The right eye was involved in 158 cases (49.2%) and the left eye in 163 cases (50.8%).

Table 2: Visual Acuity Characteristics and Time of Presentation of Rhegmatogenous Retinal Detachment, Menelik II Hospital, Addis Ababa, Ethiopia, October 2013 - February 2016(N=321)

	Male (N)	Female (N)	Total N (%)
Presenting visual acuity			
<3/60	192	88	280 (87.2)
< 6/18, > 3/60	29	7	36 (11.2)
6/6 – 6/18	3	2	5 (1.6)
Time of presentation			
< 1week	14	4	18 (5.6)
1- 4 weeks	60	23	83 (25.9)
5 –12 weeks	56	31	87 (27.1)
13 –24 weeks	43	19	62 (19.3)
>24 weeks	51	20	71 (22.1)
Causes of delayed presentation			
Distance	55	28	83 (25.9)
Lack of awareness	27	19	46 (14.3)
Late referral	58	21	79 (24.6)
Financial constraints	16	6	22 (6.9)
Long appointments	54	19	73 (22.7)
Others	14	4	18 (5.6)
Total	224	97	321

Due to ocular media opacity, it was not possible to examine the posterior segment in 35 eyes (10.9%). Out of 286 eyes with clear media, 268 eyes (93.7%) had macula off detachment. Four retinal quadrant involvement in 98 eyes (34.3%). The break(s) responsible for the RRD were identified in 188 eyes (65.7%). Of these 188 eyes, the RRD was attributed to a single break in 141 (75.0%).

Horse-shoe tears and atrophic breaks were found in 127 (67.6%) and 31 (16.5%) cases respectively. The break was localized to the superotemporal and superonasal quadrants in 91 (48.4%) and 45 (23.9%) of eyes respectively (Table 3).

History of spectacle use for myopia was elicited in 151cases (47.0%). History of ocular trauma was found in 101 cases (31.5%) and of these, in 90 (89.1%) the trauma was described as blunt. Fifty-two cases (16.2%) had undergone major ocular surgery, of which cataract surgery accounted for the majority 49 (94.2 %).

Of those who had undergone cataract surgery, pseudophakia and aphakia accounted for 80.3% and 19.7% respectively (Table 1) The mean age for traumatic retinal detachment was 37.3 years and for non-traumatic RRD it was 44.3years. The difference was statistically significant (p-value=0.013).

Table 3: Clinical Characteristics of Rhegmatogenous Retinal Detachment, Menelik II Hospital, Addis Ababa, Ethiopia, from October 2013 to February 2016. (N=321)

	Sex		
	Male (N)	**Female (N)**	**Total N (%)**
Macula status			
On	14	4	18(5.6)
Off	185	83	268 (83.5)
Hazy view	25	10	35(10.9)
Extent of RRD			
One quadrant	4	1	5 (1.6)
Two quadrants	56	28	84 (26.2)
Three quadrants	66	33	99 (30.8)
Four quadrants (total)	73	25	98 (30.5)
Hazy view	25	10	35 (10.9)
Breaks found			
Yes	133	55	188(58.6)
No	66	32	98(30.5)
Hazy view	25	10	35(10.9)
Type of breaks			
Horse-shoe tears	92	35	127(39.6)
Atrophic breaks	20	11	31(9.7)
Giant tears	10	8	18(5.6)
Dialysis	11	1	12(3.7)
Not seen	91	42	133(41.4)
Location of breaks			
Supero-temporal	60	31	91(28.3)
Supero-nasal	36	9	45(14.0)
Infero-temporal	23	11	34(10.6)
Infero-nasal	14	4	18(5.6)
Not seen	91	42	133(41.4)

DISCUSSION

This is the first large prospective descriptive study on RRD in Ethiopia and one of few such studies in Africa. The mean age of our study subjects was 41.8 years, comparable to that of a study from India which had a mean age of 38 years (4) and another study from South Africa which reported a means age of 40 years (5). Our study participants however were on average younger than what has been reported from studies conducted in some western countries. Studies from Minnesota in the United States (6), Finland (7) and New Zealand (8) each reported a mean age of 54 years while in Sweden the mean age was 60 years (9). The younger age of patients with RRD in developing countries may reflect the demographics which is dominated by young people. It may also be a result of RRD developing at a younger age in developing countries. It has been reported that RRD develops at a younger age among African Americans (10).

The role of gender in RRD development remains obscure in many reports. It has been thought that there might be a sex difference among patients with RRD with a preponderance of males even when cases with traumatic RRD are excluded. Reports from East Africa (11), Minnesota (6), New Zealand (8), Singapore (12) and Scotland (13) have shown male predominance in the incidence of RRD. In this study, males had a three-fold higher rate of RRD than females, with this tendency observed across almost all age groups. However, as this study is not a population-based study, the gender difference may reflect gender bias in accessing health care services rather than increased epidemiologic risk of the disease in males.

Because of poorly developed primary eye care infrastructure and limited facilities for the diagnosis and management of retinal diseases in the developing world, many patients with RRD present late.

The proportion of patients presenting within the prognostically favorable first week of onset of symptoms is only 5.6%, with 68.5% of patients presenting later than 1 month after onset of symptoms. In India (4) 44% of patients were symptomatic for over a month before presentation while in Iran this figure was 47% (14). In South Africa 70% of eyes had symptoms for at least one month prior to surgery (5). The mean duration of detachment of our patients was much longer than their European counterparts. Distance from the tertiary center (25.9%), late referral from primary centers (24.6%) and long appointment (22.7%) were the three major reasons our patients gave for not coming early.

Myopia is a well-known risk factor for RRD. The Eye Disease Case Control Study showed that myopic people have 4-10 times higher risk of developing RRD (15). A significant proportion of RRDs (47%) in our patients was associated with myopia. The prevalence of myopia in our series was higher than a previous report from India where it was 18.4% (4).

In our study, trauma was thought to contribute to the RRD in 31.5% of the cases. Similarly, trauma contributed to the RRD in 30% of eyes in South Africa (5). In developed countries, trauma was found to contribute less with a report of 7% from Minnesota (6).

In South Africa 9.6% of eyes with RRDs had previous cataract surgery (5). That proportion of eyes that had undergone cataract surgery was 24.1% in Kenya (11), 12% in Singapore (12), 27.5% in Iran (14) and 35.7% in India (4). The proportion of patients with RRD following cataract extraction in our study was 15.2% which is comparable to East African studies (11). With increased effort to increase cataract operations, the proportion of RRDs associated with cataract surgery is bound to increase. This will be compounded by the increased risk of RRD in complicated cataract surgeries which are bound to happen in the setting of limited infrastructure and less than optimal training.

Macular attachment at presentation is an important prognostic indicator of visual outcome after reattachment surgery. Western studies showed a macula-off detachment rate of 40-60%, (4,9) compared with a higher rate of 86.8% in developing countries (16). Our series has shown the highest proportion of macular detachment (93.7%), which is consistent with the high rate of late presentation (94.4%). High rate of total and near total detachments with preponderance of macula-off cases was observed from other African countries (5,11).

Nearly 71.1% of our patients had total or near total retinal detachment with three or four quadrant involvement. In contrast, in a large series from Scotland, four quadrant involvements were found in only 8% of cases (13).

The causative break was identified only in roughly 65.7% of eyes, in whom the media was clear. This is in sharp contrast with the theoretical teaching where the proportion of patients in whom the responsible break(s) are identified is well above 90%. One important reason for the lower detection rate of breaks is that since many patients present late with complicated RRDs which are deemed inoperable, limited effort is made to find the breaks in these cases. At the time of the study, the most common procedure was scleral buckle surgery with vitrectomy surgery being done in very few cases. Thus, many of the RRDs were judged to be inoperable, thus reducing the break detection rate.

In our series, a horseshoe tear was found in 67.5% of RRDs in which retinal breaks were detected. This figure is very high when compared to a South African study where only 28% of RRDs were caused by horseshoe tear with Posterior Vitreous Detachment (PVD) and 29% due to atrophic holes (5). Regarding location of breaks, in most cases, the retinal breaks were in the supero-temporal quadrant (48.4%), the next common site being in the supero-nasal quadrant (23.9%). A large study from Scotland reported the supero-temporal quadrant as the most common site (56.0%) followed by the supero-nasal quadrant (25.7%) (13).

Most of the subjects with RRD seen in our study presented very late to the study center during the study period so that a significant number of eyes (69.5%) showed signs of longstanding RRD at presentation. This figure by far exceeds the reports from other countries such as 33% from South Africa (5), 32% from India (4) and 13% from Iran (18).

Conclusion

This study has shown that RRD occurs at a younger age among Ethiopians. High myopia, blunt ocular trauma and cataract extraction in decreasing order were the main risk factors predisposing Ethiopians to RRD. Patients with high myopia need regular follow up with dilated fundus evaluation to detect retinal breaks early. Ocular trauma in general should be addressed by delivering health education to the community using mass media, at schools and health care facilities. The study also showed that most patients with RRD seek medical attention quite late with features of long-standing retinal detachment at first presentation to a health facility.

Hence adopting measures such as increasing access to vitreo-retinal services by decentralization of such services to the regions and ensuring that facilities are well equipped and increasing the number of vitreo-retinal surgeons in the country is highly recommended.

Competing interest

The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

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ORIGINAL ARTICLE

AN INSIGHT INTO THE CIRCLE OF WILLIS, ITS VARIATION IN THE FORMATION AND COMPONENT VESSELS IN THE ADULT HUMAN CADAVERS

Prasanna LC, MD[1*], Andrade LS, PhD[1], Ravichandra P, MD[1], Hosapatna M, MD[1]

ABSTRACT

Introduction: *Circle of Willis, is an arterial circle, furnishing arterial supply to most of the brain and meninges. It is formed by the branches of anterior cerebral, middle cerebral and posterior cerebral arteries. However, its formation and a complete arterial circle, differs among individuals.*
Objectives*: In the present study, an attempt has been made to identify those variations and to segregate them into anterior and posterior circulation.*
Methods*: Thirty-two cadaveric brains were used for the study. The circle of Willis was identified and painted for better visualisation and then photographed.*
Results: *The results show that the variations of the anterior circulation exceeded those observed in the posterior circulation.*
Conclusions: *These variations would add on to the previous findings and thus help the neurosurgeons while operating this region.*
Key words: *Anterior cerebral artery; basilar artery; brain, cadaver; circle of Willis; communicating artery; internal carotid; posterior cerebral*

INTRODUCTION

The optimum functioning of an individual at any given point of time is highly dependent on constant neural activity going on in the brain, which reflects the high metabolic activity and the amount of energy requirement. This enormous demand is met with through a profuse network of blood vessels called the circle of Willis/circulus arteriosus cerebri which serve to convey an uninterrupted supply of nourishment and oxygen to the brain (1).

The circle is formed by the terminal branches of internal carotid and vertebro-basilar arterial systems in the interpeduncular fossa at the base of the brain. Although a complete circular channel almost always exists, one vessel is usually sufficiently narrowed to reduce its role as a collateral route rendering the circle functionally incomplete (2,3). The cerebral and communicating arteries may be absent, hypoplastic, double or even triple (4,5).

Considering the complexity of the developmental pattern in arterial circle, arterial variations occur mostly because of absence of a vessel normally present or abnormal persistence of an embryonic stage of a vessel (6).

Keeping in view the surgical importance of this region, the present study was undertaken to observe the formation of the Circle of Willis, in terms of origin and branching pattern of the component vessels, to evaluate any variations in the component vessels, and to note the frequency of occurrence of different patterns of variant circles (in terms of anterior and posterior circulations). The study not only adds clinically significant unreported variations to the literature but also finds out the prevalence of these variations in the study population.

MATERIAL AND METHODS

Thirty-two cadaveric specimens were procured from the routine dissection done for the undergraduate students in the Department of Anatomy, Kasturba Medical College, MAHE, Karnataka, India. After cleaning and carefully removing the overlying meninges without damaging the vessels, the pattern of formation and the existing anatomical variations of the constituent vessels of the circulus arteriosus cerebri was noted. Each specimen was photographed using a digital camera with the variations noticed. The observations were carried out by a single person. Ethical clearance was obtained from the institutional ethical committee (IEC). The number of the ethical clearance is IEC 331/2012.

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RESULTS

Among the 32 cadaveric specimens observed for the formation of circle of Willis, 15 (46.9%) specimens show the normal description of symmetric polygon architecture without hypoplasia or aplasia. The remaining 17 (53.1%) showed variant formative patterns which ranged from complete absence of vessels to presence of extra vessels.

Among the variant circle, three (9.4%) circles were found to be incomplete of which two were found to be open in the posterior part (Figures 1a and 1b) and one in the anterior part of the circle (Figure 1c).

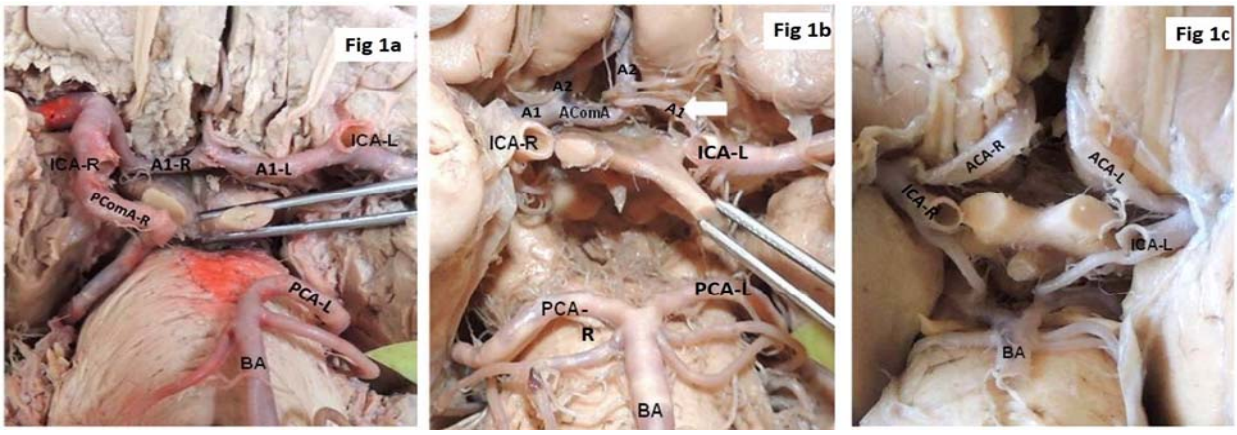

Figure 1: Open circle of Willis

Fig. 1a: Open posterior part of circle of Willis with absent P1-R and PComA-L

Fig. 1b: Open posterior part of circle of Willis with bilateral absent PComA

Fig. 1c: Open anterior part of circle of Willis with absent AComA

BA – Basilar artery, PCA-L – left posterior cerebral artery left, PCA-R – Right posterior cerebral artery right, ICA-L – Left internal carotid artery, ICA-R – Right internal carotid artery, PComA – Posterior communicating artery, AComA – Anterior communicating artery, ACA – Anterior cerebral artery.

Twelve specimens (37.5%) were found to have a variant Anterior Communicating Artery (AComA). Absence of the vessel constituted the most common anomaly. Among the six (18.7%) circles with absent AComA (Figure 1c), one was open with no communication between the two anterior cerebral arteries and no clear-cut demarcation between A1 and A2 segments of the anterior cerebral artery (ACA) of each side (Figure 1c).

The remaining five showed fused ACAs of both sides which united at the site of AComA and then redivide to continue their course as A2 segments (Figure 2a).

Next common variation seen was duplication of the AComA, of which three (9.4%) were observed (Figure 2b). The other variations seen of the AComA were network type of arterial vessels in the region of AComA as seen in one case. Y-shaped anterior circulation (Figure 1b) was seen in two cases one on each side.

In this type of anterior circulation, the AComA and the A2 segments of both sides seem to be fed by A1 segment of any one side either left or right. Occurrence of aneurysm was seen in one specimen (3.125%) in the region of junction between ACA and AComA. None of the observed specimens showed hypoplasia (<0.5mm diameter).

Among the cadaveric specimens, five (15.6%) variant types of ACA were found. Unilateral hypoplastic (Figure 1b and 3a), fenestrated (Figure 3b) and duplicated (Figure 3c) types were seen in one (3.1%) specimen each. Two specimens showed asymmetry of the ACAs in terms of diameter on the left and right sides. Anterior cerebral arteries arising from the internal carotid arteries of the respective sides are divided into a precommunicating part (designated as A1) and a post communicating part (designated A2) by the presence of an AComA. The A1 segments of the two sides along with the AComA constitute the anterior circulation.

Figure 2: Circle of Willis showing different types of AComA
Fig 2a: Absent AComA with fused ACAs in its place indicated by white arrow
Fig 2b: White arrows indicate duplicated AComA

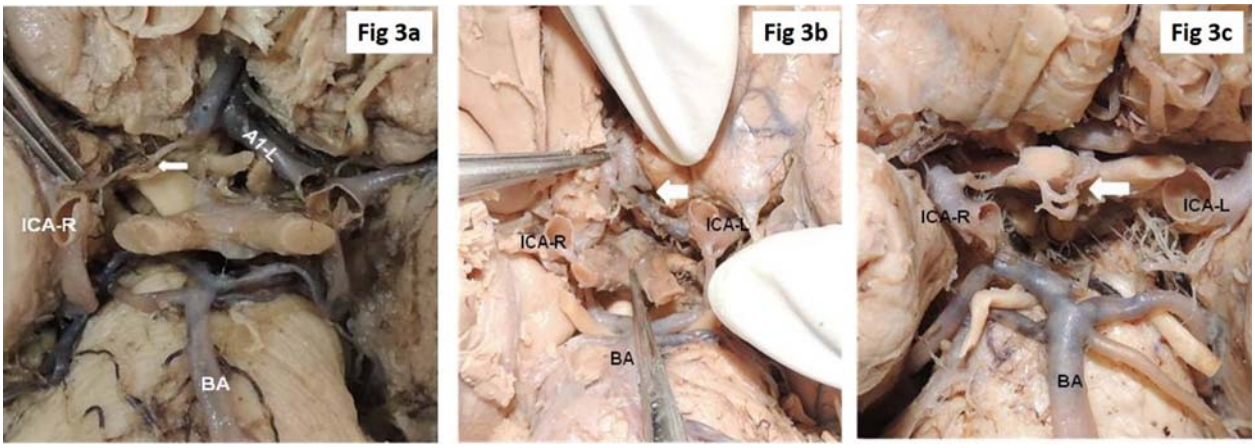

Figure 3: Variations observed in ACA
Fig. 3a: White arrow indicates hypoplastic A1-R segment
Fig. 3b: Fenestrated A1-L segment indicated by the white arrow
Fig. 3c: Duplicated A1-R segment indicated by white arrow

Only eight (25%) specimens showed variations of the PComAs. Among the variant PComAs, four (12.5%) were found to be unilateral (Fig. 1a) and the remaining four bilateral (Figure 1b). Among the unilateral variations, one was completely absent (Figure 1a) and one hypoplastic (Figure 4a), two were found to be network type (Figure 4b). Among the bilateral variations, one was completely absent (Figure 1b) with an open circle of Willis.

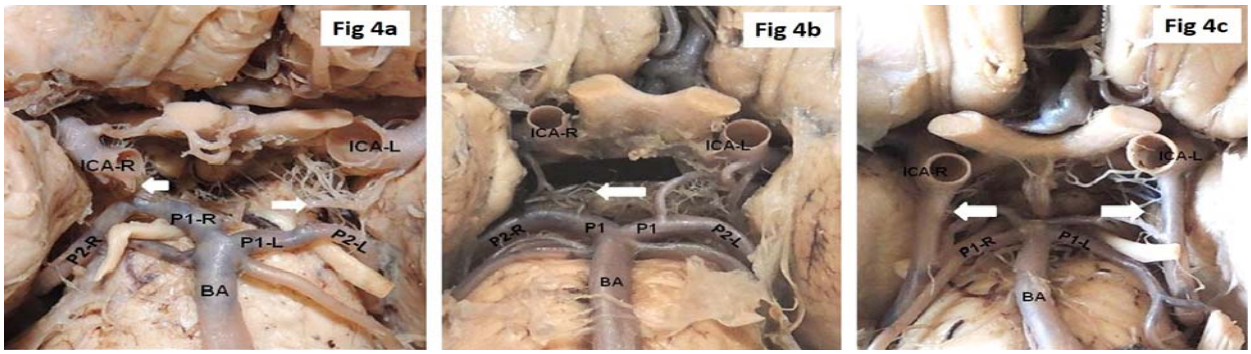

Figure 4: Types of PComAs observed
Fig. 4a: White arrows indicate hypoplastic PComA
Fig. 4b: Network type PCom-R indicated by white arrow
Fig. 4c: Bilateral fetal type of PComA indicated by white arrows

Bilateral absence of PComAs was seen in two cases. Only 2 (6.3%) out of the 32 studied cadaveric specimens showed variations. Both were unilateral and presented with complete absence (Figure 1a) of the vessel either in the right or left side. One of the two variations were the incomplete circle of Willis, awhile the other circle was completed by direct communication of the PComA with the basilar artery in place of absent PCA.

DISCUSSION

The cerebral arterial circle of Willis has shown to have a wide range of variations from 4.6% to 72.2% (4,5,7,8). It could be due to the sheer number of vessels involved in its formation or different methods of assessing its formation, and disparate nomenclature given to component vessels by different authors and hence an attempt has been made to describe the variations in terms of anterior and posterior circulations.

Most of the workers have reported that the normal Circulus Arteriosus is present in only 50% or less of the cases. Windle reported that 59.5% circles had normal arrangement of arteries in the circle of Willis (6) Fawcett & Blackford (1905) documented 96.1% of complete circle of Willis. (3) Bergmann mentions that textbook description of normal and symmetrical Circulus Arteriosus is true in only 34.5% of the cases (4). Overall in the present study the anterior circle variations were found to be more when compared to the posterior part indicating the posterior part of the circle enjoyed better circulation (7)

Previous authors have found that the anomalies of the circle are more common in the posterior part as observed in Table 1.

Table 1: comparison of Posterior part of circle of willis between the previous authors and present study

Author	Variations - anterior part	Variations - posterior part
Saeki et al (8)	-	49%
Jain et al (9)	29.6%	51.4%
Van (10)	29%	81%
Gunnal (5)	40%	50%
Present study-cadaveric	25.0%	15.6%

Circulus Arteriosus: Anterior Part

AComA-ACA Complex:

1. Anterior Communicating Artery:

In the present study, among the total AComA-ACA complexes, AComA was present and single in 62.5% of the cadaveric specimens. Double and fenestrated vessel was seen in 9.3% and 3.3% cases. The present study also showed an equal proportion of network type (3.3%) and Y-shaped (6.6%) AComA. Windle reported AComA absent in 3% and double in 3% of the cases (6).

Fawcett & Blackford reported that the artery was single in 92.1%, absent in 0.14% and double in 7.2% of the cases (3) Vare & Bansal studies showed that AComA was absent in 1.1%; double in 10.28% and AComA-ACA complex was H-shaped in 1.1% (11). Luzsa illustrated that the artery was absent in 0.3% of the cases and the occurrence of a median trunk in 1.2% of the cases (12). Osborn also reported the presence of more common azygous ACA which ranges from 0.2-4%) (13).

2. Anterior cerebral artery (A1-Segment):

In the present study, the pre-communicating anterior cerebral artery (A1 segment) was present in all the cadaveric specimens and in 96.7% of the specimens. It was found to be hypoplastic in one specimen (3.1%), fenestrated and with an asymmetric A1 segment in two specimens (6.3%) each. Windle reports the absence of the artery in 1% (6). Luzsa report states the absence of the artery in 0.7 - 11% and hypoplasia in 8 - 15% (12). Osborn states the absence of the A1 segment in 1 - 2% (13). Macchi and Stephen & John also reports 2% hypoplasia of the A1 segment (14,7). Kane reports 9.61% each of aplasia & hypoplasia of A1 segment (15).

3. Posterior communicating artery (PComA):

In the present study, the PComA was found to be absent in approximately 6% of the cases seen both in dissected specimens and radiological images studied. Hypoplastic PComA was seen in one (3.1%) of the specimens. Two (6.3%) specimens showed network type PComA.

PComA arising from basilar artery was seen in 3.3%. Windle reported the vessel to be absent in 15% of the cases; both PComA were absent in 1.5%; 4.5% involving the right and 6.5% on left side and the vessel was hypoplastic in 3.5% of the cases (6). Fawcett & Blackford reported that the vessel was absent in 0.4% on both sides; absent on the right side in 1.8% and on the left side in 1.4% of the cases (3).

Riggs mentions bilateral hypoplasia of PComA in 11% and unilateral hypoplasia of PComA in 6% of the cases (16). Jain reports indicated that the artery presented maximum anomalies in 50% of the cases (9). Stephen & John (1991) mentions the absence of posterior communicating artery on one side in 23% cases (7). In Macchi et al., hypoplasia of the PComAs was noted in 21% of the cases (14). Osborn mentions hypoplasia or absent PComA in 25-33% (13). Merkkola et al., reported absence of PComA in 46% (17). Eftekhar et al., reports the absence of PComA on both sides in 3%; right side in 4% and left side in 3% of the cases (18). Bilateral hypoplasia of PComA was seen in 33%; unilateral hypoplasia of PComA was observed in 27% out which, right side was 16% and left side was in 11% of the cases.

5. Posterior Cerebral Artery (P1Segment):

In the present study, the pre-communicating artery (P1 Segment) was present in 30 out of the 32 specimens (93.8%) and absent in two cases (6.3%). It was hypoplastic in two cases (6.3%), one on each side. The artery originated from the terminal bifurcation of the basilar artery in 26 (86.7%) cases. In four cases (13.3%) the artery originated from Internal carotid artery (ICA), two cases on each side accounting for 6.7% each.

Windle study shows an anomalous P1 segment in 13.5%; PCA originating from ICA on the right in 5.5% of the cases and left in 2% of the cases (9). Fawcett & Blackford study indicates that the artery had an abnormal origin, arising from ICA in 0.14%; 0.9% on the right and 0.57% on the left (3). Riggs' study showed that the unilateral hypoplasia of P1 present was present in 16% of the cases (16). Vare & Bansal studies show 25% P1 segment anomalies having an abnormal origin from ICA and 5.7% of the cases had both P1 segments arising from the ICA; 13.7% on the right and 5.7% on the left. [11] Stephen & John illustrated 14% of the posterior cerebral arteries arising from Internal carotid with P1 being hypoplastic on the same side (7) Macchi showed 2% of the cases had P1 segment arising from the ICA (14). Osborn illustrations show 15-22% hypoplastic P1 segment (13).

Conclusion:

It is noteworthy that most of the above described variations of the component arteries do not occur in isolation but are seen in various permutations and combinations attributing to a highly versatile range of types circles of Willis. The communicating arteries remained the most important vessels which helped maintain collateral circulation.

Competing interest:

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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ORIGINAL ARTICLE

INTRAPARTUM GROUP B STREPTOCOCCI COLONIZATION AND SEROTYPE DISTRIBUTION AMONG MOTHER NEWBORN DYADS AT TIKUR ANBESA SPECIALIZED HOSPITAL, ETHIOPIA

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ABSTRACT

Introduction*: Group B streptococcus was identified as the leading cause of neonatal disease in developed countries. There is scarce data from developing countries. The surrogate for early-onset neonatal disease caused by Group B streptococcus is the rectovaginal colonization of pregnant women before delivery.*

Objective*: to determine the Group B streptococcus colonization rate among pregnant women and their newborns, vertical transmission rate and serotype distribution at Tikur Anbessa Specialized Hospital.*

Method: *A hospital based cross-sectional study was conducted at Tikur Anbessa Specialized Hospital from March 2015 to August 2015. Two hundred eighty pregnant women and their newborns were screened for Group B streptococcus. Isolated Group B streptococcus were serotyped by using serotype-specific antisera. A structured questionnaire was used to collect socio-demographic and obstetric data. Logistic regression was used to compare the Group B streptococcus colonization rate with different factors. A P value less than 0.05 was taken as a test of significance.*

Result: *Group B streptococci colonization rate among pregnant women, newborns and vertical transmission rate in this study were 65(23.2%), 95% CI [18.6-28.9], 32(11.3%), 95% CI [7.8-14.8] and 32/65(49.2%) respectively. Type Ia Serotype was the most commonly identified GBS isolated in the present study.*

Conclusion: *Group B streptococci colonization rate detected in this study was high. Serotype Ia was the predominant serotype followed by serotype II. In the future, we recommend studies to determine the burden of early-onset diseased that could be caused by GBS in the study area.*

Keywords: *Group B streptococcus, Vertical transmission, Colonization rate, Serotype, Ethiopia*

INTRODUCTION

Group B Streptococcus (GBS) remains a major cause of morbidity and mortality among newborns in many countries (1). Rectovaginal colonization of pregnant women during and before delivery is a prerequisite for the development of early-onset disease (EOD) (2). Factors such as prolonged rupture of membrane, prematurity, chorioamnionitis, low level of anti-GBS capsular antibody and previous newborn with EOD can increase the risk of EOD (3).

Intrapartum antibiotic prophylaxis (IAP) can prevent vertical transmission of GBS from colonized pregnant women to their newborns, and there are two main way to select pregnant women for IAP: screening and risk factor-based approaches (4). The Centers for Disease Control and Prevention (4) recommends that all pregnant women between the 35 and 37 gestational weeks should be screened for GBS colonization, and for those with positive cultures antibiotic should be administered.

In some countries, IAP is administered based on the presence of clinical risk factors such as preterm labor, premature or prolonged rupture of membranes, GBS bacteriuria, and previous infant with GBS disease (5).

Penicillin G is the drug of choice for prophylaxis with ampicillin as the alternative medication (6). For pregnant women who are allergic to penicillin but without a history of anaphylaxis, cefazolin is the preferred antibiotic. Vancomycin is recommended for those with a history of anaphylaxis, and if GBS is resistant to erythromycin and clindamycin. If GBS is susceptible to erythromycin or clindamycin, either of them is recommended for IAP (7).

As a result of IAP, the burden of EOD caused by GBS has declined dra-matically over the past 15 years in the USA and other developed countries (7, 8). IAP is not commonly used in most developing countries including Ethiopia.

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Even though IAP has substantially reduced the incidence of disease, it has its own limitation. The strategy does not eliminate all cases of the disease; it does not affect late-onset disease caused by GBS and there is a concern of the selection of antimicrobial resistant bacteria.

Above all, it is not feasible for developing countries including Ethiopia, where resource is limited for laboratory diagnosis. As an alternative, a capsular based vaccine is being developed; currently, vaccine formulation containing Ia, Ib, and III is in a clinical trial and it was reported to be cost-effective (9). However, as GBS serotypes vary from place to place and from time to time the current vaccine formulation on trial may not work for all countries. As a result, comprehensive data on GBS stereotypes is required.

The contribution of GBS in neonatal mortality and morbidity in Ethiopia was not well addressed and there is also scarce information regarding maternal and neonatal GBS colonization, vertical transmission rate, and serotype distribution. In the study substantial, colonization and vertical transmission was reported (10). Therefore, this study was done with the objective of providing data about Group B streptococci colonization rate among mothers and newborns and vertical transmission rate including its serotypes distribution.

PATIENTS AND METHODS

Study design, Period and Area

A hospital-based cross-sectional study was conducted from March 2015 to August 2015 at Tikur Anbesa Specialized Hospital (TASH). TASH is in Addis Ababa which is the capital city of Ethiopia; the hospital is located at the center of the country, with a total population of 3,384,569 (11). TASH is a tertiary referral, teaching governmental hospital and the largest of all public hospitals in Ethiopia. The hospital has a total of 800 beds, 80 of which are currently being used in obstetrics and gynecology ward. About 3000 deliveries are attended each year and 60% of these are operative deliveries.

Study population and sample size calculation

The sample size was calculated by using a single proportion formula, margin of error = 0.05, Confidence interval = 95%, prevalence of 20.86% from the previous study conducted in Ethiopia (12). Based on the calculation the sample size was 280; convenient sampling technique was used to recruit study participants. Two-hundred eighty pregnant women who were in labor at TASH and their newborns were screened for GBS. Newborns were followed through telephone for 7 days to check about their health status.

Inclusion and exclusion criteria

We included pregnant women with vaginal delivery and who were willing to participate in the study along with their newborns. Pregnant women who were on antibiotics and with planned cesarean section were excluded.

Variables of the study

Dependent variable: GBS colonization rate
Independent variables: Factors that could be associated with maternal and newborn GBS colonization rate.

Sample collection, handling, and transport

Swabs from the lower vagina and the rectal region of women in labor and external ear, nasal area, throat and umbilical area of the newborn were collected by trained attending midwifery. All sample collection was done according to the recommendation of the Center of Disease Control and prevention (4). All swabs were placed on Stuart's transport media (BD Diagnostics, USA) and were delivered to the Microbiology Laboratory within 4 hours.

Culture and identification of GBS

Rectovaginal swabs from pregnant women and swabs from the external ear, nasal, throat and umbilical area of newborn was placed into Lim broth (BD Diagnostics, USA) supplemented with colistin (10µg/ml) and nalidixic acid (15µg/ml). The purpose of an antibiotic is to prevent the overgrowth of commensals. The inoculated selective medium was incubated for 18–24 hours, at 37^{o}C in 5% CO_2 enriched atmosphere and then sub-cultured onto sheep blood agar and incubated in 5% CO_2 enriched atmosphere at 37^{o}C for 18−24 hours. If GBS was not identified after the incubation of 18–24 hours, blood agar plate was re-incubated and examined at 48 hours to identify suspected organisms.

All suspected GBS colonies (beta-hemolytic, or non -hemolytic, Gram positive cocci, catalase-negative) were sub-cultured and isolated for confirmatory testing. A CAMP (Christite, Atkins, Munch, Petersen) test was considered presumptive identification of a positive GBS culture. Ambiguous CAMP test culture results were re-tested using a Strp B Grouping Latex (Remel, USA). GBS isolate was serotyped by using-type specific antisera (Statens Serum Institute).

Statistical analysis

Data entry and analysis was done using SPSS version 20 software. Prevalence figures were calculated for the total study population and separately by age group and risk factors. Logistic regression was used to compare the results obtained from pregnant women and their newborns with different age groups and risk factors. A P value of less than 0.05 was considered statistically significant.

Ethical approval and consent to participate

The study was approved by the Institutional Review Board of the College of Health Sciences, Addis Ababa University (Ref No: 069/13/DMIP) and the National Ethics and Research Committee (Ref No: 3.10/795/06). Written informed consent was obtained from all study participants. The parents also consented for permission to collect samples from their newborns.

RESULTS

Socio-demographic characteristics

A total of 280 pregnant women along with their 283 newborns participated in the present study. Majority of the participants were from Addis Ababa city and most of the participants were housewives and were in the age group of 25-29 (Table 1). Mean age was 26.6 with Standard deviation of $\pm$4.5.

Table 1: Socio-demographic characteristics of pregnant women attending Tikur Anbessa Specialized Hospital, Addis Ababa, March 2015 - August 2015 (n=280)

Variables	Description	Frequency	Percent
Address	Addis Ababa	220	88.6
	Outside Addis Ababa	60	21.4
Occupation	Housewives	190	67.9
	Private work	60	21.4
	Government employee	23	8.2
	Student	7	2.5
Age	15-19	23	8.2
	20-24	103	36.8
	25-29	115	41.1
	30-34	27	9.5
	35-39	11	3.9
	40-44	1	0.4
Sex of newborn	Male	158	55.8
	Female	125	44.2

Gestational characteristics of pregnant women and newborn

Pregnant women

Among 280 pregnant women participated in the present study, 223(79.6%) delivered at gestational age of 37-42, 147(52.5%) were multigravida; 32(11.4%) had history of newborn with EOD; 129(46.1%) had history of spontaneous vaginal delivery (SVD); most of them had a duration of rupture of the membrane of 0-5 hours; 14(5%) had a premature rupture of membrane (PROM) (Table 2). All mothers recruited in this study were alive, mode of delivery was vaginal, no complication associated with GBS colonization was observed.

Newborns

From a total of 283 newborns participated in this study, those who were alive during birth were 270 (95.4%); most were in the weight range of 2500-4000g; the majority of them had APGAR score at 5 minutes >7; 257(90%) newborns had APGAR score at 10 minutes >7; 18(6.4%) newborns had other abnormalities (Table 3).

Table 2: Gestational characteristics of 280 pregnant women attending Tikur Anbessa Specialized Hospital, Addis Ababa, March 2015 - August 2015 (n=280).

Characteristics		Frequency	Percent
Gestational age in weeks	<37	37	13.2
	37-42	223	79.6
	>42	20	7.1
Gravida	Primigravida	133	47.5
	Multigravida	147	52.5
History of EOD	Yes	32	11.4
	No	115	41.1
	NA	133	47.5
Previous mode of delivery	Vaginal	129	46.1
	CS	18	6.4
	NA	133	47.5
Duration of rupture of membrane (In the index pregnancy)	0-5 hours	179	63.9
	6-10 hours	66	23.6
	11-15 hours	35	12.5
PROM	Yes	14	5
	No	266	95
Chorioamnionitis	Yes	1	0.4
	No	279	99.6
Meconium stained amniotic fluid	Yes	9	3.2
	No	271	96.8
Other illness*	Yes	35	12.5
	No	245	87.5

EOD: early onset disease, NA: not applicable, SVD: spontaneous vaginal delivery, CS: Cesarean section, PROM: Premature rupture of membrane

*HIV/AIDS, Patent ductus Arteriosus, Epilepsy, Thrombocytosis, Cord prolapse, Diabetes mellitus

Table 3: Clinical characteristics of newborn delivered at Tikur Anbessa Specialized Hospital, Addis Ababa, March 2015 - August 2015 (n=283).

Characteristics		Frequency	Percent
Newborn status during birth & immediate after birth	Alive	270	95.4
	Dead	13	4.6
Weight	<1500 gram	16	5.7
	1500-2499 gram	31	11.1
	2500-4000 gram	236	83.4
APGAR score at 5 minutes	<7	83	29.3
	>7	200	70.7
APGAR score at 10 minutes	<7	26	9.2
	>7	257	90.8
Developed EOD	Yes	6	2.1
	No	277	97.9
Other abnormality*	Yes	18	6.4
	No	265	93.6

APGAR: Appearance, Pulse, Grimace, Activity, Respiration EOD: early onset disease

*Clift lip and palate, Hydrocephaly, Down syndrome, Spina befida.

GBS colonization rate among mothers and newborns

Group B streptococcus colonization rate among pregnant women was 65(23.2%), 95% CI [18.6-28.9]; GBS colonization among newborns was 32 (11.3%), 95% CI [7.8-14.8]. Among GBS colonized newborns none of them developed sign and symptoms of early onset disease but one of them was stillbirth.

GBS serotype distribution and vertical transmission rate

Vertical transmission rate of GBS from pregnant women to their newborns in the present study was 32/65(49.2%); overall serotype distribution of GBS was: Ia 22(22.7%), Ib 16(16.5%), II 29(29.9%), III 7(7.2%), V 18(18.6%), none-typeable 5(5.2%) (Table 4).

Table 4: Serotypes distribution of GBS isolated from pregnant women and their newborn and vertical transmission rate at Tikur Anbessa Specialized Hospital, Addis Ababa, March 2015-August 2015

Serotype	Pregnant women	Newborn	Pregnant women & newborn	VTR
Ia	14/65(21.5%)	8/32(25%)	22/97(22.7%)	8/14 (57.1%)
Ib	10/65(15.4%)	6/32(18.8%)	16/97(16.5%)	6/10 (60%)
II	19/65(29.2%)	10/32(31.3%)	29/97(29.9%)	10/19 (52.6%)
III	4/65(6.2%)	3/32(9.4%)	7/97(7.2%)	3/4 (75%)
V	15/65(23.1%)	3/32(9.4%)	18/97(18.6%)	3/15 (20%)
NT	3/65(4.6%)	2/32(6.3%)	5/97(5.2%)	2/3 (66.7%)
Total	65	32	97	32/65(49.2)

Risk factors associated with GBS colonization rate

Group B streptococci colonization rate among mothers and newborns in the current study was not significantly associated with any of the risk factors measured.

DISCUSSION

Prevalence of GBS colonization among pregnant women is not consistent across different regions (1,2). GBS colonization rates vary during pregnancy; colonization late in pregnancy is a good predictor of GBS transmission from mother to newborn and that could lead to EOD (1,4). In the present study, maternal and neonatal GBS colonization rate and vertical transmission rate were 23.2%, 11.3%, and 49.2% respectively.

Comparison of GBS colonization rate among different studies was usually biased by methodological differences (4). Maternal GBS colonization rate in this study was higher compared to some African countries, such as Nigeria (13), Mozambique (14) but it is similar to colonization rate reported from Ghana (15), Congo (16) and Malawi (17).

In contrast to our study, higher colonization rates have been reported previously from Europe (14) and 47% from Zimbabwe (18).

Like many other studies, maternal GBS colonization rate found in this study was in the range of 10 -30% (19,-21) and it was high compared to the colonization rate reported from Brazil 14.6% (22), Germany 16% (23); it is comparable to the colonization rate reported from Sweden, 25.4% (24), and Malawi, 21.7% (25). There are several reasons for the differences observed in colonization rate such as; laboratory methods used, site and time of sample collection.

Newborn GBS colonization rate (11.3%) and vertical transmission rate of GBS from mother to newborn (49.2%) found in this study was comparable with earlier studies conducted in United States (2). In this study, 1 out of 32 GBS colonized newborn was stillbirth. Recently some studies reported that colonization with GBS may lead to stillbirth (26), this area may need further investigation in Ethiopia setting. In this study, a significant association was not found between maternal and newborn GBS colonization rate and the risk factors ($P>0.05$).

Group B Streptococcus (GBS) serotype distribution vary from one region to the other (27) and it will also change over time (28, 29) however, serotype III, Ia, Ib, II, and V are the common GBS serotypes reported from developed countries (29,30). In this study, serotype II (29.9%) was predominant followed by Ia (22.7%), V (18.6%), Ib 16.5%, and III 7.2%. Our finding was comparable with GBS serotypes reported from other countries (31); however type III was less prevalent but highly transmissible in this study compared to report from other countries (1,7,9,31). Like our study low serotype III prevalence was reported from Brazil (2) and Japan (28).

Other studies also reported that serotype III to be the most common (48.9%) among different geographic areas, followed by serotypes Ia, Ib, II, and V (31). These five serotypes account for more than 94% of neonatal diseases caused by GBS worldwide (30). The reason we did not find newborn with early onset disease can be due to small sample size, the nature of GBS strains in the study area, and antibody in maternal antibody.

Limitations

Since we have used a convenience sampling technique, it may cause a selection bias. Mothers who were asked about the health status of their newborn may not provide correct information.

Conclusions

In this study, we found a high GBS colonization rate among pregnant women and their newborns at TASH. This indicates the existence of primary risk factors for EOD in the study area. The prevalent GBS serotypes we identified in this study were serotype II, Ia, V, Ib, III. Therefore, we recommend further study to identify the burden of neonatal disease due to GBS in the study area.

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Competing interests

The authors declare that this manuscript was approved by all authors in its current form and that no competing interest exists.

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ORIGINAL ARTICLE

CLINICAL PROFILE AND PATTERNS OF EXTREMITIY FRACTURES IN ORTHOPEDICS DEPARTMENT IN TIKUR ANBESSA SPECIALIZED HOSPITAL

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ABSTRACT

Introduction: *Bone Fracture and other Musculoskeletal injures continue to be important causes of morbidity, disability and mortality both in the developed and developing countries. Around the world, 5.8 million people every year (1,600/Day) die from injuries.*

Objective*: The aim of this study was to assess the clinical profile and patterns of extremity fractures in patients visiting the Orthopedic Department of "Tikur Anbessa" Specialized Hospital (TASH) in Addis Ababa.*

Method*: Institution-based retrospective study was carried out. The study participants were extremity fracture patients who visited Orthopedic Department of TASH. The sample size was 354.Data was collected using structured checklist. Medical record numbers (MRNs) were obtained from health management information system (HMIS) record and daily morning sheet through systematic random sampling method. The data were analyzed using Chi-square ($\chi 2$) test.*

Results*: Study participant consisted 251(73.6%) male and 90 (26.4%). Most of the victims, 111 (32.6%), were between the age of 15 and 29 years. Lower extremity fracture (65.6%) was more common compared to upper extremity (34.7%). Femur was the most commonly fractured bone (23.7 %). The common patterns of fractures were transverse type (35.5 %). The leading cause of fractures was road traffic injuries (RTIs) (42.2%). The Cause of fracture and number of fracture were significantly associated with age ($p<0.05$).*

Conclusion*: The most commonly fractured single bone is the femur. Transverse factures were the commonest patterns of fracture. The leading cause of fracture was road traffic injury.*

Keywords*: Extremity, fracture, Patterns, "TikurAnbessa" Specialized hospital, TASH, Black Lion, Ethiopia*

INTRODUCTION

A fracture is a loss in the structural continuity of bone which results from injury, repetitive stress, or abnormal weakening of the bone (a pathological fracture). Most fractures are caused by sudden and excessive force, which may be direct or indirect (1). It is the most common pattern of orthopedic injuries, which affects all age group and frequently associated with other injuries (2). Fracture prevalence differs in different parts of the world and that the spectrum of fractures presenting to different hospitals may vary considerably (3).

Globally, injury continues to be an important cause of morbidity, disability and mortality both in the developed and developing countries. Around the world, 5.8 million people die every year, and about 16000 people die from injuries every day (4). Among persons aged 15 through 44 years, injuries account for 6 of the 15 leading causes of death. Road traffic injuries (17.5%), falls (12.2%), interpersonal violence (10.1%), and self -inflicted injuries (9.7%) are the main injury-related cause. RTA is the 10th leading cause of death and the 9th leading cause of the burden of disease (5).

The Global Burden of Disease (GBD) estimated that combined rates of extremity injury from falls and road traffic crashes ranged from 1000 to 2600/100,000 per year in most low-and middle-income countries (LMICs) compared with 500/100,000 per year in high income countries (HICs) (two to five times higher in LMICs) (6,7).

In developing countries some data indicates a huge burden of disability from musculoskeletal injuries. Some of these data come from individual country studies, such as a population-based survey showed that 0.83% of Ghanaians had an injury-related disability. The vast majority (78%) of such disabilities were due to extremity injuries. Hence; extremity injury related disability is alerting issue in developing countries (8).

Hospital based studies continue to show the effect of injury on the continuity of bone, and that it is a major cause of morbidity and mortality in Africa. For instance, in Nigeria out of patients treated for fracture and dislocation, lower limb and upper limb fractures occurred in over 70% and 20% of cases, respectively (9).

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Despite the increasing trend suggested by available data, bone injuries especially extremity injuries have not received the attention they deserve in most developing countries including Ethiopia (10). Therefore, the aim of this study was to investigate patterns of extremity fractures and to identify its mechanism of injury in "Tikur Anbessa" Specialized Hospital (TASH), Addis Ababa, Ethiopia.

PATIENTS AND METHOD

Study area: The study was conducted in Tikur Anbessa Specialized Hospital (TASH, Black Lion) Department of Orthopedics, Addis Ababa, Ethiopia.

Study design: Institution-based cross-sectional study design was employed, with retrospective data collection form charts of patients with extremity fractures records from December 2016 to December 2017.

Source and study population: The source population was all fracture patients who visited Orthopedic Department in TASH beginning from December 2016 to December 2017. The study population was all extremity fracture patients presented to orthopedics department in TASH that fulfill the inclusion criteria. Extremity fracture patient charts that had incomplete data greater than 20% of the variables, charts which were lost from record office at the time of data collection and fracture in children resulting from birth trauma were excluded from the study.

Sample size determination: There was no published data on the prevalence of extremity fracture in all age groups in Ethiopia. Therefore, the estimated prevalence of extremity fracture is 50%. The minimum number of sample required for this study was determined by using single population proportion formula. Since the sample was taken from a relatively small population which was 2002, there was a need for sample size correction formula. As a result, 10% was added for incomplete data. Thus, the final sample size was set at 354.

Sampling procedure: The medical record number (MRN) of all patients with a diagnosis of fracture was collected from emergency and regular fracture clinic health management information system (HMIS) registration book of the hospital within study period. The inpatient registration book and daily morning sheets also were checked to avoid missing of some unregistered charts in HMIS of emergency and fracture clinic. During collection of MRNs of patients with fracture, extremity fracture patients were selected and then numbers were assigned, respectively, according to registration date in HMIS. According to the number of cases distribution in pediatric and adult age group, the sample size was determined proportionally for each age group. Systematic random sampling method (every 5^{th}MRN) was used to take sample in each age group. The initial starting MRN was identified by a simple random sampling method (lottery method) to take sample systematically in each group.

Data Collection Tool and Procedures: Data was collected using structured checklist which was adapted from previous literature. MRNs were obtained from HMIS record and daily morning sheet through systematic random sampling method to get the main file of the patient from patients chart room. Finally, based on the inclusion and exclusion criteria of the study, cards which had important variables for the study were used. Then, data regarding all variables were collected from the main card.

Data analysis and Interpretation: The data were checked after each data collection for its completeness. The data was entered onto Epi-Data version 4.2 and then exported to SPSS Version 21 for analysis. For categorical data, descriptive statistics like frequency and percentage were computed and presented by way of tables and graphs. Continuous variables were summarized using means, median, mode and standard deviation. Chi-square ($\chi 2$) test was applied to see if there was any association between the different categorical variables related to fracture. Statistically significant association was declared at p-values <0.05.

Ethical considerations: Ethical clearance was obtained from Research Ethics Review Committee (DRERC) of Department of Anatomy, School of Medicine, College of Health Science, Addis Ababa University and TASH Outpatient Department Director. Confidentiality of patient information was maintained through taking the data anonymously. After data collection, the raw data including personal identifiers was secured and was not accessed by anyone except the principal investigator and to keep confidentially.

RESULTS

Out of the total fracture patients (2,002) who visited orthopedic department in TASH, 354 extremity fracture cases were sampled in the present study. Of the 354 sampled cases, 341 had complete patient charts data and thus, data analysis was based on 341 cases. The study participants comprised of 251 (73.6%) males and 90 (26.4%) females resulting in a male to female ratio of 2.8:1 (Table-1). The median and the mode ages of participants' age were 24 and 35 years, respectively. Most of the injured 111 (32.6%) were between the ages of 15 and 29 years (Table-1).

Table 1: Age and sex distribution of patients with extremity fractures, Tikur Anbessa Specialized Hospital, Addis Ababa (N=2002).

Characteristics		Frequency	Percent
Gender	Male	251	73.6%
	Female	90	26.4%
Age	0 – 14	103	30.2%
	15 – 29	111	32.6%
	30 – 44	55	16.1%
	45 – 59	27	7.9%
	60 – 74	27	7.9%
	>_ 75	18	5.3%

In this short review, lower extremity was the most common site of fracture (65.6%) compared to upper extremity (34.7 %). The most commonly fractured bone in the lower extremity was the femur 89 (23.7%), followed by tibia and fibula together 49 (13.0%). The least fractured bone was phalangeal bone 1(0.3%).

The femur was also the most affected bone in the skeleton of extremity. In the upper extremity, the most commonly fractured bone was the humerus, 36 (9.6%), followed by radius and ulna together 30 (8.0%) while the scapula was the least fractured bone which accounted for only 2 (0.5%) (Table 2 and Table 3).

Table 2: Frequency and pattern of upper extremity fractures, Tikur Anbessa Specialized Hospital, Addis Ababa (N=2002).

Fractured bones	Frequency	Percent
Scapula	2	0.5%
Clavicle	7	1.9%
Humerus	36	9.6%
Radius and Ulna	30	8.0%
Only Radius	22	5.9%
Only Ulna	23	6.1%
Carpal	3	0.8%
Metacarpal	4	1.1%
Phalangeal	3	0.8%
Total	130	34.7%

Table 3: Frequency and pattern of lower extremity fractures, Tikur Anbessa Specialized Hospital, Addis Ababa (N=2002).

Fractured bones	Frequency	Percent
Pelvic	48	12.8%
Femur	89	23.7%
Patella	7	1.9%
Only Tibia	39	10.4%
Only Fibula	4	1.1%
Tibia and Fibula	49	13%
Tarsal	3	0.8%
Metatarsal	6	1.6%
Phalangeal	1	0.3%
Total	246	65.6%

The majority of fractures were simple (closed) type, 282(82.7%), followed by compound (open) type 55 (16.1%). A total of 303(68.3%), had single fracture and multiple fracture patients accounted for 108 (31.7%).

The common pattern of fracture was transverse,121 (35.5%), followed by comminuted, oblique, mixed, spiral, and greenstick which accounted for 79 (23.2%), 67 (19.6%), 39 (11.4%), 22(6.5%), and 13 (3.8%), respectively (Table 4).

Table 4: Specific patterns of extremity fractures, Tikur Anbessa Specialized Hospital, Addis Ababa (N=2002).

Pattern	Frequency	Percent
Transverse	121	35.5%
Oblique	67	19.6%
Comminuted	79	23.2%
Greenstick	13	3.8%
Spiral	22	6.5%
Mixed*	39	11.4%

**multiple site fracture cases who had different patterns of fracture*

RTI was observed to be the leading cause of extremity fractures and accounted for 144 (42.2%) followed by fall accident, 101 (29%) (Table 5).

Table 5: The prevalence of causes of fracture, Tukur Anbessa Specialized Hospital, Addis Ababa (N=2002)

Causes	Frequency	Percent
Road traffic injury	144	42.2%
Falling down accident	101	29.6%
Gunshot injury	10	2.9%
Occupational related injury	10	2.9%
Sport related injury	19	5.6%
Assault / direct blow	40	11.7%
Pathological	15	4.4%
Others	2	0.6%
Total	341	100%

Out of 144 (42.2%) road traffic injury victims, pedestrians were the most vulnerable group and accounted for 62 (43.1%) followed by passengers and drivers:52 (36.1% and 30 (20.8%), respectively (Fig 1).

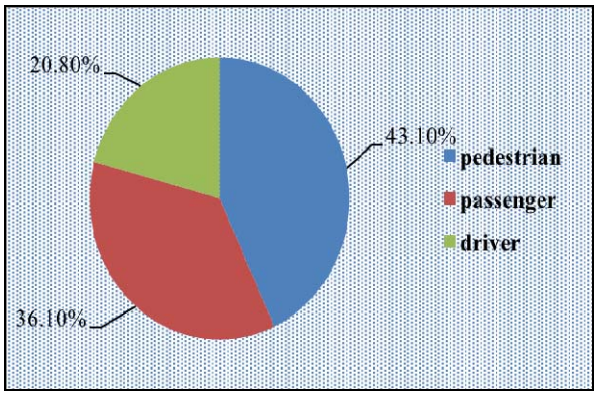

Figure 1: Victim groups by RTI in patients with fractures, Tukur Anbessa Specialized Hospital, Addis Ababa (N=2002).

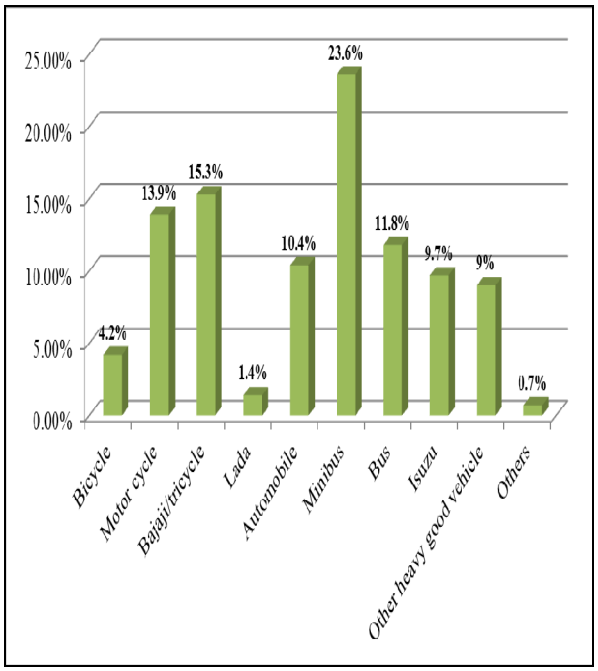

Figure 2: Frequency of the types of vehicles that are involved in road traffic injury, Tukur Anbessa Specialized Hospital, Addis Ababa (N=2002).

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The causes of fracture in the various age-groups were significantly different. Out of 144 road traffic injury patients, the most common types of vehicle involved in road traffic injury was the minibus 34 (23.6 %), followed by 'Bajaji'/Tricycle, 22(15.3%) %) (Figure- 2).

DISCUSSION

The results of this simple review revealed that lower extremity fractures (65.6%) were significantly higher compared to upper extremity (34.7%).This observation is in agreement with a study conducted in Karnataka, India, where lower extremity fractures (60%) were more common compared to upper extremity (31%)(12).

However, the finding of the present study were inconsistent with reports of a study carried out in Munipar, India, where upper extremity fractures (58.6%) were more common compared to lower extremity (41.83%) (13). One reason for the difference may be the fact that the common cause of fracture in the current study was RTIs in contrast to a study conducted in Munipar, India, where the most common causes were falling down accidents. In falling down accidents, the upper limb may be used as a defense or protection scheme to minimize the severity of injury.

The present study also contradicts the reported data of the investigation conducted in Wolaita, Southern Ethiopia, where upper limb fracture was more common (46.4%) than lower limb fracture (37.5%) (11). This inconsistency may be due to the fact that, in the study in Wolaita, most of the RTIs were attributed to motorcycles and Bajaji/Tricycles where as in the current study the most common RTI involved Minibuses. Moreover, the sample size used in the study in Wolaita was smaller compared to that in the present study. In the study in Wolaita, RTIs were also the common cause of fracture.

Our investigation revealed that the most commonly fractured bone in the extremity was femur (23.7%), followed by tibia and fibula together (13%). In the upper extremity, humerus was the most commonly fractured bone (9.6%). This finding is in line with reports of studies conducted in India and Nigeria (12, 14) as well as with a reported data of the investigation in TASH, Ethiopia (15, 16). However, the prevalence of femur fracture in the current study was higher. Patient referrals to TASH was much higher during the current investigation than that during the earlier studies carried out in TASH in 2009 and 2010 (15, 16).

The majority of fractures were simple (closed) type, 282(82.7%), a total of 303(68.3%), had single fracture and common pattern of fracture was transverse,121 (35.5%). These facts encourage to plan for day-case surgery using IM locking nails, hence avoiding admissions.

Furthermore, fractures were observed to occur more in males (73.65%) compared to females (26.4 %) resulting a ratio of 2.8:1. This ratio was comparable to that reported by a study conducted in Munipar, India; where male to female ratio was 2.7: 1(13). The possible explanation for the high prevalence of fracture in males may be their high activity levels and linkage in high-risk activities. Most of the victims were between the ages of 15-29 (32.6%).

This finding is consistent with a study carried out in kashan, Iran, where the most affected groups were between the ages of 15-29 (43.2%) (17). The possible reason for this finding may be the fact these age group represents the most productive and reproductive age group and therefore, economically and socially active, participating in higher levels of economic and high-risk activities. However, the prevalence of fractures in the current study for this age group was relatively small compared to that reported in the Iran study. The reason for the difference in the findings may be the use of a relatively smaller sample size in the current study compared to the study conducted in Iran.

In our study, the most common causes of extremity fractures in all age group was RTI (42.2%) followed by falling down accidents (29.6%). This finding is in agreement with a reported data of investigations carried out in Nigeria (9, 21) and in India (19, 20), where RTI was identified as the most common cause of extremity fractures. However, the prevalence of RTI in the current study was smaller as compared to that reported by the Nigerian study (72%), (73.2%) and the Indian study (59.72%), (62%). The possible explanation for this discrepancy may be the difference in sample size, (smaller in the present study), in the number of people actively involved in motor vehicle related activities and in the number of motor vehicle. On the other hand, the prevalence of RTIs in the present study was higher as compared to that reported by the study carried out in Wolaita , Southern Ethiopia, (35.4 %) (11). The current study was conducted in TASH, a tertiary hospital for the country and sample size used was larger.

In the present investigation, most of the victims of RTI were pedestrians (43.1%), followed by passengers (36.1%). This finding is consistent with a reported data of an investigation conducted in Kenyatta national hospital, Kenya (23). However, the finding of the current study contradicts results of a study carried out in Pakistan, where drivers (68%) followed by passengers (32%) were the most affected population groups (22). The high prevalence of RTIs observed in pedestrians, in the present study, may reflect the low level of community awareness on road traffic safety and road use. In addition, the absence of pedestrian walkways in most of the roads in Addis Ababa, Ethiopia, may have contributed to the higher vulnerability of pedestrians to motorized vehicles. Therefore, educating the public on RTIs and safe use of the roads is critical.

Moreover, the types of vehicle that were mostly involved in road traffic injury in the present study were minibuses (23.6%) followed by Bajaji/tricycle/ (15.3%). This finding is in agreement with a study carried out in Kenyatta national hospital, Nairobi, Kenya, where minibuses also were the type of vehicle mostly involved in RTIs (23). The possible reason for this may be to the fact that, in these two cities, the majority of people use minibuses as the main transportation means.

Conclusion: Transverse femur fracture was a commonest, hence day-case based surgery using IM locking nails is highly recommended to avoid long stays and hospital admission. The leading cause of fracture across all age groups was RTI (road traffic injury) and most of the victims were young male pedestrians. Public awareness on traffic rules and regulations should be enhanced in the schools as well as in the media to minimize this problem.

National, multicenter, prospective and randomized studies with large sample size should be conducted in order to influence decision and policy makers further. Furthermore, health professionals working in the hospitals should properly and completely document patients' medical information.

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ORIGINAL ARTICLE

RETINOPATHY OF PREMATURITY - AN EMERGING CAUSE OF CHILDHOOD BLINDNESS IN ETHIOPIA

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ABSTRACT

Introduction: *Retinopathy of prematurity is an increasing cause of blindness in children in low income countries as neonatal services expand.*
Objective: *To describe the characteristics, stage of retinopathy of prematurity and treatment outcomes in preterm infants attending a tertiary eye center.*
Methods: *Review of medical records from June 2016 to December 2019. Data on birthweight, gestational age, postmenstrual age at presentation, age at first examination, stage of retinopathy of prematurity , and treatment outcomes were extracted and analysed.*
Results: *Thirty three of 93 (35.5%) infants had retinopathy of prematurity : vision-threatening 21 (22.6%); two with aggressive posterior retinopathy of prematurity, or Stage 4/5 (n=12). The mean (±SD) gestational age of these 33 infants was 29.1 (±1.9) (range 26-33) weeks; mean (±SD) birth weight was 1185.6 (±234.5) (range 680–1800)g. Treatments were: anti-VEGF injection (n=6), LASER (n=1), anti-VEGF and LASER (n=1), lens-sparing vitrectomy (n=1), lensectomy with vitrectomy (n=1), LASER and lensectomy with vitrectomy (n=1). In 18 cases retinopathy of prematurity regressed (11 spontaneously, 7after treatment), and one failed follow up. One progressed to stage 4 and 12 (10/93, 12.9%) were blind or visually impaired.*
Conclusions: *Preterm infants at risk of retinopathy of prematurity are now surviving in Ethiopia. There is a need to increase awareness and establish retinopathy of prematurity screening and treatment services, with wide screening criteria initially to determine the population at risk of vision threatening retinopathy of prematurity .*
Key words: *Preterm birth, low birth weight, Retinopathy of prematurity, childhood blindness, Ethiopia.*

INTRODUCTION

Retinopathy of prematurity (ROP) is a vision-threatening disease associated with abnormal retinal vascular development at the boundary of vascularized and avascular peripheral retina of preterm babies (1). The main risk factors for ROP are prematurity, low birth weight and hyperoxia from poorly regulated use of supplemental oxygen (2, 3). The first case reports of retrolental fibroplasia, as ROP was called then, were described by Terry in Boston, in the United States of America in 1942 (4).

Since then ROP has become a leading cause of avoidable blindness in children in most regions of the world. The World Health Organization's Vision 2020 initiative, which was launched in 1997, identified ROP as an important emerging cause of blindness in children, particularly in the middle-income countries of Latin America, Eastern Europe, and Asia (5). In 2010 it is was estimated that every year 32,300 preterm infants become blind or visually impaired (1).

More than 60% of the world's 15 million preterm births occur in South Asia and Sub-Saharan Africa (6). Until recently there were limited data regarding the incidence of ROP in Africa. However, in the last decade, there has been an increasing number of published reports which show that ROP is emerging in some African countries. ROP screening guidelines are in place for only two countries in Africa (South Africa and Kenya)(7), yet the systematic review by Wang D *et al* showed that there are published data on ROP from six African countries including South Africa, Egypt, Nigeria, Sudan, Rwanda and Kenya(8).

There have been three epidemics of blindness due to ROP since it was first described in the 1940s (9). The first two occurred in high income countries (USA and Western Europe): the first epidemic was due to the use of unmonitored 100% supplemental oxygen, and the second was due to greater survival of increasingly preterm infants.

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The third epidemic of ROP began in the 1990s in the middle income countries of Eastern Europe, Latin America and South East Asia due to the increased survival of premature infants as a result of expansion of intensive neonatal care services (10). However, neonatal care was often of inadequate quality, and coverage of ROP screening and treatment services was low (7,9).

The third epidemic has already started in South Africa, an upper middle income country, and other countries in the region are considered to be the next frontier for ROP epidemics as a result of increasing economic development and expanding neonatal care (7).

Ethiopia, the second most populous nation in Africa, has a preterm (<37 weeks of gestation) birth rate of 10% and a low birth weight rate (babies born <2,500g) of 20%. Every year 320,000 babies are born preterm (11). The two previous studies in schools for the blind in Ethiopia (published in 2003 and 2017) reported no cases of ROP blind children at that time (12, 13). However, Wang D *et al* in their review postulated that there are a number of populous countries with comparable health systems to those for whom there are published data in Africa, where it is likely that ROP will emerge, such as Ethiopia, Democratic Republic of Congo, and Tanzania (8).

In this study we report a series of preterm infants with ROP for the first time in Ethiopia, and the outcomes of treatment. The infants were all examined in a private tertiary eye center in Addis Ababa, Ethiopia.

PATIENTS AND METHODS

A center-based, retrospective review of records was undertaken of all premature infants who attended the WGGA eye center between June 1, 2016 and December 31, 2019. The study protocol was approved by WGGA eye center ethics review committee. Data were extracted from the electronic medical records using a pre-designed check list, including mode of referral, birthweight (BW), gestational age (GA), postmenstrual age (PMA) at presentation, postnatal age at first examination, the number of days on oxygen, diagnosis and stage of ROP, method of treatment if required, and treatment outcomes. Data were entered into Microsoft Excel, and exported into and analyzed using Epi info 7 software.

Examination was conducted immediately on arrival at the outpatient pediatric ophthalmology and strabismus clinic. All infants were examined for ROP by one pediatric ophthalmologist initially (MA), and those with a diagnosis of ROP were also examined by a retina specialist (AK). Pupillary dilatation was achieved using a mydratic cocktail of 0.5% cyclopentolate and 2.5% phenylephrine or 1% tropicamide plus 2.5% phenylephrine instilled three times every 5-10 minutes. After instillation of topical anesthesia (0.5% proparacine hydrochloride ophthalmic solution), an Alfonso newborn eyelid speculum was inserted, and a Flynn scleral depressor was used to rotate the eye. Funduscopic examination was by indirect ophthalmoscopy (Keeler Spectra Iris) using a 28D Volk© lens. Retinal changes were classified according to the most advanced stage of ROP using the International Classification of ROP (14).

If vascularization was incomplete, infants were seen at 2-weekly intervals until mature retinal vessels were confirmed, or ROP developed. Infants with ROP were seen at weekly intervals until regression or Type 1 ROP was noted. Type 1 ROP was defined as any stage of ROP in zone I with plus disease; zone I, stage 3 ROP without plus disease; or zone II, stage 2 or 3 ROP with plus disease (15). Those with Type 1 ROP received either confluent LASER peripheral photocoagulation to the avascular retina or anti-vascular endothelial growth factor (VEGF) (Avastin, Lucentis or Eylea) injection within 48 hours of diagnosis. Those with Type 2 ROP (Stage 1-2 without plus disease in zone I, Stage 2-3 without plus disease in zone II) were followed up weekly until regression of ROP or until vascularization into zone III was achieved. Lens sparing vitrectomy or lensectomy and vitrectomy surgery were performed for stage 4 and selected cases of stage 5 ROP.

RESULTS

Ninety-three preterm infants were included in the study; 53 (57%) were female and 17 (18.3%) were from multiple births. Most infants (87.1%) were referred for ROP screening by pediatricians from three private neonatal units. Two infants with stage 4 ROP were referred for treatment by an ophthalmologist from a government university hospital. The remaining 10 cases were brought by parents seeking a solution for the abnormal visual behavior they had noticed in their child (Table 1).

The mean (±SD) GA was 30.9 (± 2.5)(range 26-40) weeks and the mean (±SD) BW was 1500.2 (± 491.7) (range 680-3900) gram. Mean (±SD) age at first examination was 10.3 (±15.4) (range 2 -116) weeks and the mean (±SD) PMA (GA plus chronological age) was 40 (±9.3) (range 31 -90) weeks.

Table 1: Characteristics of infants with retinopathy of prematurity presenting to WGGA Eye Center, Addis Ababa, Ethiopia, from June 2016 to December 2019 (N =33)

						Eye with most advanced ROP				
	How referred	**GA**	**BW**	**Days in oxygen**	**PMA at presentation (weeks)**	**Stage**	**Zone**	**Plus**	**Treatment**	**Outcome**
1	Self	26	ND	ND	90	5			None	Blind
2	Self	26	1200	ND	62	5			None	Blind
3	Self	30	900	30	55	5			None	Blind
4	Self	29	1350	32	57	5			None	Blind
5	Self	28	1150	ND	68	5			None	Blind
6	Self	28	1000	30	56	5			None	Blind
7	Self	28	1400	ND	60	5			None	Blind
8	Self	29	1100	ND	53	4			None	Blind
9	Self	27	1300	54	59	5			None	Blind
10	Self	ND	ND	ND	ND	5			None	Blind
11	Ophthalmologist	32	1800	12	48	4			PPV	VI
12	Ophthalmologist	28	1000	60	44	5			PPV/lensectomy	VI
13	Pediatrician	27	1130	56	35	3	1	Yes	Laser/PPV/ lensectomy	Progressed to Stage 4, VI
14	Pediatrician	27	1400	14	32	APROP	-	Yes	Avastin	Regressed
15	Pediatrician	32	1070	15	36	APROP	-	Yes	Lucentis	Regressed
16	Pediatrician	29	1000	63	53	3	2	Yes	Avastin	Regressed
17	Pediatrician	27	680	77	40	3	2	Yes	Laser	Regressed
18	Pediatrician	31	1350	25	34	3	2	No	Avastin	Regressed
19	Pediatrician	30	1300	30	35	3	2	Yes	Avastin	No follow up
20	Pediatrician	28	1080	35	33	3	2	Yes	Avastin	Regressed
21	Pediatrician	29	1100	30	38	3	2	Yes	Eylea	Regressed
22	Pediatrician	27	1180	ND	63	2	2	No	None	Regressed
23	Pediatrician	30	1400	0	36	2	2	No	None	Regressed
24	Pediatrician	30	1300	35	36	2	2	No	None	Regressed
25	Pediatrician	31	1300	30	37	2	2	No	None	Regressed
26	Pediatrician	31	1040	28	36	2	2	No	None	Regressed
27	Pediatrician	29	2038	33	40	3	3	No	None	Regressed
28	Pediatrician	33	1800	9	36	2	2	No	None	Regressed
29	Pediatrician	29	1200	20	43	3	2	No	None	Regressed
30	Pediatrician	30	1100	7	34	1	2	No	None	Regressed
31	Pediatrician	29	900	60	ND	1	3	No	None	Regressed
32	Pediatrician	26	1000	35	31	2	2	No	None	Regressed
33	Pediatrician	31	1185	25	36	2	2	No	None	Regressed

ND = no data; APROP =Aggressive posterior ROP; PPV= pars plana vitrectomy; VI =visually impaired; PMA = Postmenstrual age

Among infants referred by a pediatrician for ROP screening (n=81), the mean (±SD) age at examination was 6 (± 4.9) (range 2 – 36) weeks and mean (±SD) PMA was 37.2 (± 4.2) (range 31-63) weeks. Fifty-five babies (55/81, 62.9%) were examined between 25 – 40 days of age. Twenty-one of these 81 infants (25.9%) developed ROP and ten (12.3%) needed treatment. The mean (±SD) age at examination for self-referred cases was much higher [42.0 (±28.7), range 20 -116 weeks] than those referred by pediatrician ($\chi 2$ =102.1, p <0.001). Among the 93 infants included in the study, 33 (33/93, 35.5%) were diagnosed with ROP, 21 of whom (21/93, 22.6%) had vision-threatening and 12 (12.9%) had mild ROP.

The mean (±SD) GA of these 33 infants was 29.1 (±1.9) (range 26-33) weeks; mean (±SD) BW was 1185.6 (±234.5) (range 680–1800) gram. Twenty-one infants (22.6%) had vision threatening ROP (i.e., any Zone I disease (n=1), Stage 2 or 3 disease in Zone II with plus disease (n=6), two had aggressive posterior ROP (APROP) and 12 had Stage 4 or 5 ROP). The mean GA of these 21 infants was 28.6 ± 1.8 (range 26 – 32) weeks, mean (±SD) BW was 1174.2 (± 239.4 (range 680-1800) grams, and the mean (±SD) PMA at presentation was 48.7 (±14.9) (range 32-90) weeks. Figure 1 shows the distribution of BW by GA for infants with vision threatening ROP, showing that all fell within the screening criteria used in the United Kingdom (GA of ≤32 weeks or BW <1501 grams) (16).

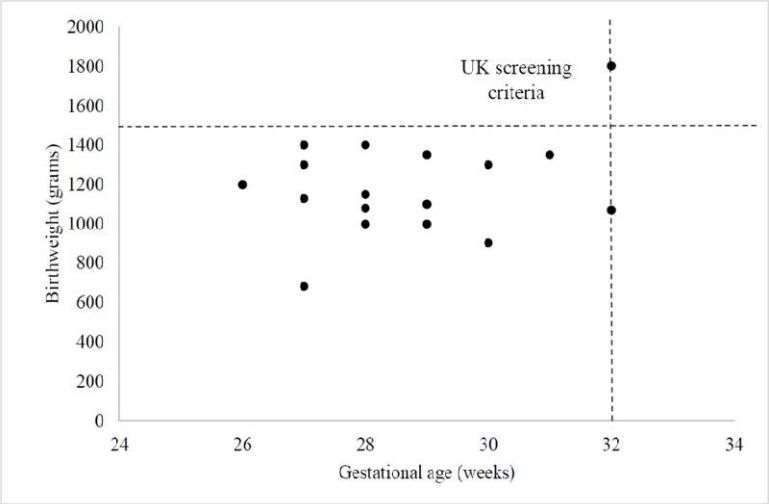

Figure 1: Gestational age and birth weight of infants with vision-threatening or Stage 4/5 ROP at WGGA Eye Center, Addis Ababa, Ethiopia (n=19; two with incomplete data).

Only 7 of the 93 (7.5%) infants did not receive oxygen, and data on the use of oxygen was not available for 10 (10.7%) cases. The mean (±SD) number of days on oxygen overall (76 infants) was 19.1 (±17.23) (range 1-77) days and was 37.5 days for infants with vision-threatening ROP, 28.2 days for those with ROP not requiring treatment, and 12.0 days for infants without ROP ($\chi 2$ =8.35, p=0.01).

Among infants with ROP, 11 (11/33, 33.3%) were treated as follows: anti-VEGF injection (n=6); peripheral LASER photocoagulation (n=1); anti-VEGF and laser (n=1); lens-sparing vitrectomy (n=1); lensectomy with vitrectomy (n=1); and LASER, then lensectomy with vitrectomy (n=1). In 18 cases (19.3%) ROP regressed (11 cases spontaneously and 7 after treatment), and one was lost to follow up. One case progressed to stage 4 despite treatment with LASER followed by pars plana vitrectomy. Twelve (12/93, 12.9%) infants were blind or visually impaired (Table 1). There was an increasing trend in the number of ROP cases: two in 2016, four in 2017, 12 in 2018, and 15 in 2019.

DISCUSSION

This study shows that preterm, very low birth weight infants are now surviving with ROP in Ethiopia. This is the result of several factors, including improved antenatal care, a higher proportion of hospital deliveries, and the recent establishment of neonatal intensive care units (NICUs) with trained neonatologists in many government and private hospitals in Addis Ababa. However, to the best of our knowledge ROP screening is not taking place in any of these units.

The finding that most cases were referred by paediatricians working in private NICUs suggests that there is some level of awareness of the need for ROP screening, at least in the private sector. However, babies were only referred from three units which may mean that the level of awareness is not uniform among all practicing paediatricians/ neonatologists in the city. Postnatal age at examination among referred cases ranged from 2 to 36 (mean 6) weeks and 62.9% were examined between 25 and 40 days of age which implies that a significant proportion of preterm babies were being referred and attended in a timely manner. In contrast, there was a marked delay in presentation among self -referred cases, as the mean age at examination was nearly one year (42 weeks), with one child presenting at over two years of age (116 weeks).

These infants had not been screened for ROP and were brought by their parents who had noticed “something white in the eyes” or a change in the visual behaviour of their child. Almost all the self-referred cases had end stage, inoperable ROP and were blind. Similar findings have been reported from Mexico, including late presentation among 48 ROP blind infants, where the median age at presentation was 5±2 (range 1-11) months (17).

In another study of 66 ROP blind infants attending a tertiary eye hospital in India, 52% were referred by an ophthalmologist and 30% were self-referred. 50% of these infants had received care in a neonatal unit without ROP screening services (18). Similar studies have not been reported from Africa.

In this study 35.5% of infants had ROP, 22.6% with vision-threatening disease, 33.3% needed treatment and 12.9% were blind. Our data cannot be directly compared to other studies in Africa where babies were all identified during screening in NICUs. In a retrospective study of screening in Kenya, 41.7% developed ROP, and 20.9% had vision-threatening disease (19). In a prospective study of 53 babies screened for ROP in Nigeria, 47.2 % developed ROP but only one developed threshold disease (20).

There is an urgent need to increase awareness and establish ROP screening and treatment services in Ethiopia. In our study no infant fell outside the United Kingdom screening criteria (16), but this may reflect selection bias, as infants may have received higher quality neonatal care in the private sector than they would have in government facilities. More studies are needed in government and private NICUs because, as in many low- and middle-income countries, larger, more mature infants may also be developing vision-threatening ROP in NICUs with less high-quality neonatal care (21). ROP screening guidelines must be locally relevant, as criteria which are appropriate in high income countries may not be applicable in low- and middle-income countries due to variation in exposure to risk factors (22). The screening criteria used in South Africa and Kenya are similar to those used in the UK, but in The Philippines, for example, the criteria are a GA of <35weeks or BW of <2000 grams (23).

A limitation of the study is that information on oxygen exposure was limited to days on oxygen, and this information came from parental recall or referral letters. The finding that the number of days on oxygen increased in line with the severity of ROP suggests that inadequately monitored supplemental oxygen may be a risk factor in this setting. Prospective studies are required, which should include awareness of the revised recommendations on optimal target oxygen saturation levels for preterm babies (90-94%), and the ability of staff in neonatal units to implement them (24).

In conclusion, this study indicates that preterm infants at risk of ROP are now surviving in Ethiopia. There is an urgent need to establish ROP screening and treatment services, to increase awareness among clinicians taking care of preterm babies and to build the capacity of ophthalmologists in screening and treatment. Although indirect ophthalmoscopic retinal examination is the standard for examining the retinae of infants, wide-field imaging for screening is gaining popularity. This is especially relevant in countries that lack ophthalmologists able to screen for ROP (25). Wide screening criteria should be used initially to delineate the population at risk of vision threatening ROP in this context. More studies on the prevalence and risk factors for ROP in NICUs are highly recommended.

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CASE SERIES

AN OUTBREAK OF CANDIDEMIA AMONG HOSPITALIZED NEONATES AT TIKUR ANBESSA SPECIALIZED TEACHING HOSPITAL: A CALL FOR INCREASED AWARENESS

Tinsae Alemayehu, MD[1]

ABSTRACT

Introduction*: Candida species are a prominent cause of hospital-onset blood-stream infections. Newborns and infants are notable risk groups. The clinical course of 17 neonates who developed hospital acquired Candidemia at Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia is described in this article. Because of diagnostic limitations hitherto, fungemias hadn't been given due attention in the hospital.*

Objectives: *The objective for this case series is to describe the presentation, diagnosis and management of newborns diagnosed with candidemia at the Tikur Anbessa Specialized Hospital, Addis Ababa.*

Methods: *A case series documented by charting the presentation and management of neonates diagnosed with Hospital-onset Candidemia from January – August 2018 is described. Extracted data was summarized using descriptive statistics (frequencies).*

Results: *Eleven female and six male newborns were diagnosed with Hospital-onset Candidemia. Thrombocytopenia featured prominently in their lab work-up. The patients took a mean of thirteen days of parenteral antibiotics before diagnosis, which was confirmed by blood cultures. Seven had C. albicans and ten had non-albicans Candidemia.*

Conclusion*: The illness and treatment course of 17 newborns treated for Candidemia at the Tikur Anbessa Specialized Teaching Hospital, Addis Ababa, Ethiopia, are charted. Awareness on risk factors and prevention is of utmost importance to limit the high mortality associated with Invasive candidemia.*

Key words: *Candidemia, Ethiopia, Newborns, Infants, albicans, non-albicans*

INTRODUCTION

Candida species are the fourth most common cause of blood-stream infections (BSIs) in intensive care. They are also among the top ten causes of community onset BSIs (1). Predisposing factors include prolonged hospitalization, use of broad-spectrum antibiotics, newborns (particularly pre-terms and those with low birth weight), abdominal surgery, immune-compromise, critical illness, hemodialysis and acute necrotizing pancreatitis (2).

The incidence of Candidal BSIs in sub-Saharan Africa has been rising over the past decade. An analysis of BSIs at a tertiary Kenyan hospital revealed that *Candida* were the most common causes (34%) of hospital-onset BSIs with three fourth of isolates being non-*albicans* species (3). A prospective cohort of Tanzanian children aged 7 years or less showed that Candidemia accounted for 9% of all BSIs (4).

Candida species (especially *C albicans* and *C parapsilosis*) are the third most common isolates from South African neonatal intensive care units with an attributable mortality of 46% (5,6).

While the proportion of Candidal BSIs due to *C albicans* in Africa is declining, the more difficult to treat non-*albicans* species (*C glabrata*, *C parapsilosis*, *C krusei* and *C auris)* are on the rise. This has been especially observed from hospitalized children in South Africa (8 – 9). Ben Abdeljelil et al also observed a shift towards non-*albicans* species (esp. *C parapsilosis)* among neonatal invasive candidiasis in a Tunisian hospital over the period between 1995 and 2010 (10).

Blood cultures can be used to diagnose Candidemia, albeit with a lower sensitivity and a slow turn-around time. Germ tube testing is used to confirm *C albicans* infection. It was first reported by Reynolds and Braude in 1956 and Taschdjian in 1960. *)*.

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Germ tubes are features of *C albicans* which are short, non-septate hyphae (differentiates it from most species) without constrictions at their point of origin (differentiates it from *C tropicalis)*. Their formation is associated with increased synthesis of protein and ribonucleic acid. A heavy inoculum will inhibit germ tube formation (11). *Candida* mannan antigens and antibodies have a good negative predictive value with rapid results in areas with low prevalence. More conclusive test include Polymerase chain reaction (PCR) analysis (11,12).

Candidemia in neonates is treated by Amphotericin B with Fluconazole being an alternative for newborns who haven't been exposed to it. Echinocandins serve to treat those with resistant *Candida* isolates (*C. krusei*, *C. glabrata* etc) or when newborns develop Fluconazole or Amphotericin B related toxicity. Treatment is continued for 2 weeks following negative blood cultures and symptoms' resolution in newborns without metastatic complications (13).

Though a multitude of studies have been conducted in Ethiopia concerning mucosal Candidiasis and Candiduria, there is a paucity of clinical data on invasive Candidemia – both in children and adults (7). The objective for this case series is to describe the presentation, diagnosis and management of newborns diagnosed with candidemia at the Tikur Anbessa Specialized Hospital, Addis Ababa.

PATIENTS AND METHODS

Study area

Tikur Anbessa specialized hospital is the largest tertiary referral hospital in Ethiopia. It has 800 beds and gives specialty care via a diverse array of disciplines. The neonatal intensive care unit (NICU) has 40 beds and includes preterm neonatal care, neonatal surgical

Study design

A case series documented by charting the presentation and management of neonates diagnosed with Hospital-onset candidemia from January – August 2018 is described.

Study population

All identified cases of Candidemia among neonatal ICU admissions within the eight months of January – August 2018 are analyzed.

Data collection, quality and analyses

Demographic, clinical and microbiological data were extracted from charts of affected newborns. A descriptive quantitative analysis of collected data was then made.

Ethical considerations

Photos of patients and any other identifiers were not used when analyzing clinical and microbiological data.

RESULTS

Overall, eleven female and six male neonates were diagnosed with Candidemia over an eight month period (January – August 2018); ten of which were diagnosed in the two months of July and August 2018 (Figure 1). The mean age at diagnosis was 11.8 days. All neonates were preterm deliveries with a mean gestational age of 31 weeks and 6 days and mean birth weight of 1488 grams.

Co-morbidities at the time of admission for the series of neonates were in keeping with their prematurity – Respiratory distress syndrome, Necrotizing enterocolitis and Patent ductus arteriosus. At the time of their Invasive candidemia diagnoses, the newborns had received an average thirteen days of a mean of three antibiotics. None exhibited oral candidiasis.

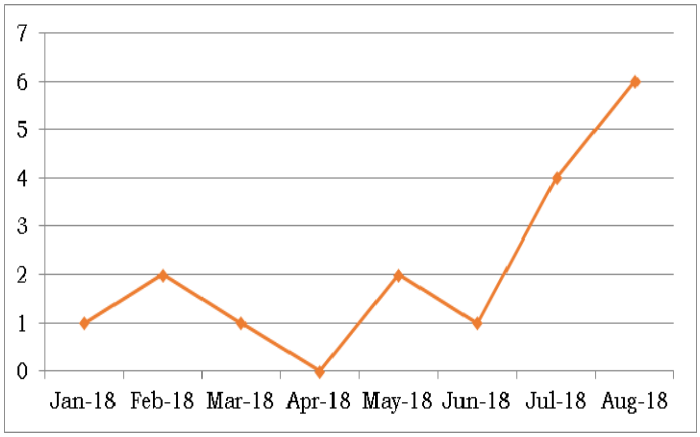

Figure 1: Diagnoses of invasive Candidemia in the neonatal intensive care unit of Tikur Anbessa Specialized hospital (January – August 2018)

Affected newborns presented with persisting fever or hypothermia, poor feeding and depressed neonatal reflexes despite respiratory support and prolonged parenteral antibiotics. The clinical diagnosis of a fungemia was based upon the fulfillment of all of the following criteria in these newborns:

- A lack of response to multiple courses of empiric antibiotic treatments
- Presence of at least one clinical risk factors for fungemia (preterm delivery, prolonged peripheral cannulization, abdominal surgery)
- Presence of laboratory predictors of fungemia like persisting unexplained anemia, leukopenia or thrombocytopenia

Quantitative serum C-reactive protein was measured in 14 of the 17 newborns and it was elevated in only a third of tests. Two-thirds (twelve) exhibited persistent thrombocytopenia (mean platelet count: 38,300/mm^3) despite negative serologic tests for other infectious etiologies like congenital toxoplasmosis, cytomegalovirus and syphilis and negative blood cultures for aerobic bacteria. Eight newborns had unexplained anemia (mean hemoglobin: 10.8 gm/dl) in serial determinations and three had persisting leukopenia (mean white blood cell count: 2,955/mm^3) for which an etiology could not be identified.

Following the fulfillment of the above clinical criteria, blood cultures were drawn with a request to observe for yeast cells after a minimum of five and a maximum of seven days of incubation.

Cure from candidemia was taken as negative blood cultures after uninterrupted antifungal treatment (in the absence of administration of antibiotics or antivirals) and clinical resolution of presenting illness.

Microbiologic procedures

Following the collection of blood culture specimens and observation of creamy white, glistening colonies on plates, gram staining was done Figure 2. A germ tube test was then performed to differentiate between *albicans* and non-*albicans* candida. With a light suspension of suspect yeast colonies made on serum in tube, the suspension was incubated at 35^0C – 37^0C for 3 to 4 hours. After a drop of suspension was placed on a slide, a wet mount was examined production of germ tubes (projections extending from yeast cells).

The presence of short, slender non-septated tubes without constriction at their point of origin confirmed a likely diagnosis of *Candida albicans* (Figures 3 and 4) and their absence was interpreted as non-*albicans Candida* blood stream infection (BSI). Further confirmatory tests on samples (e.g. *Candida* mannan antigens, PCR tests) could not be performed in the hospital's microbiology laboratories.

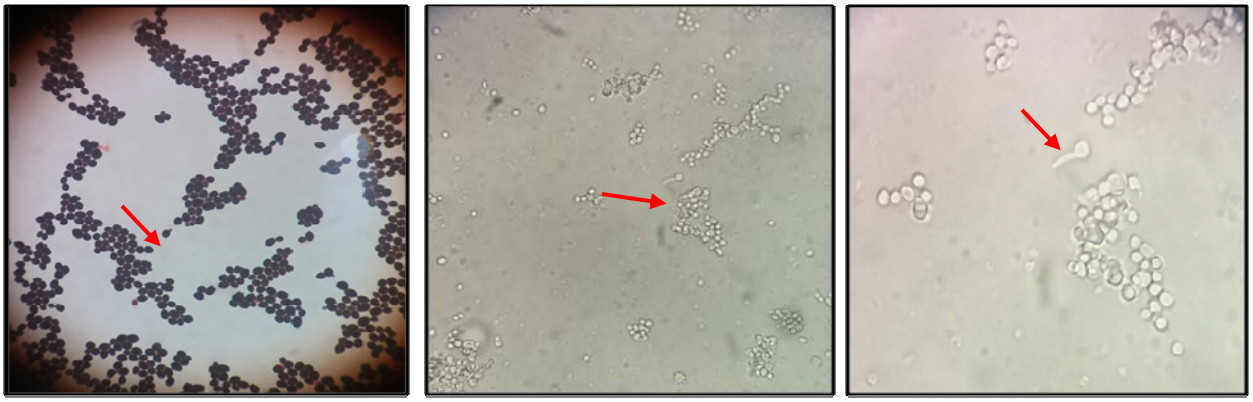

Figure 2: Gram positive budding yeasts **Figures 3 & 4** (arrows): Yeast cells with non-septate hyphae Microbiologic isolates from three newborns.

Of the isolates, ten were non-*Candida albicans* while seven were *albicans*. Anti-fungal susceptibility testing could not be done at our hospital. Based on standard recommendations for treating neonatal Candidemia (13) while monitoring availability of different anti-fungals within the hospital's pharmacy as well as privately owned medicine retail outlets, an empiric treatment with Fluconazole was planned. A shift to intravenous Caspofungin or Amphotericin B when faced with a lack of improvement in neonates with non-*albicans* species was also offered.

Four newborns improved on their illness (One with *C. albicans* sepsis and three with *C.* non-*albicans* sepsis) after being treated with a two-week course of intravenous or oral Fluconazole (while simultaneously discontinuing antibiotics) and were discharged. Two patients succumbed to their illness after starting treatment (one with a *C. albicans* isolate after three days of Fluconazole and another with a non-*albicans* isolate after being treated with three days of Fluconazole followed by eight days of Caspofungin). The rest eleven died due to an untreated Candidemia because of a lack of availability of anti-fungals in the hospitals' formulary or due to caretakers' being unable to cover the expensive costs of antifungals on sale at privately owned medicine retail outlets.

DISCUSSION

The NICU of the Tikur Anbessa specialized teaching hospital admits more than 2800 neonates per annum – averaging close to 235 per month. All confirmed candidemias from the NICU were from preterm neonates. Only four neonates survived their illness while the rest died due to a delayed diagnosis, a virulent strain or more often than not, a lack of affordable options of anti-fungal drugs. Ten newborns had sepsis due to non-*albicans Candida*. One had complicated with thrombophlebitis. The occurrence of these nosocomial neonatal infections qualifies as an outbreak in the study hospital as an increased incidence from preceding times (when diagnosis was either not considered or a limitation existed in confirming clinical diagnoses) was documented.

We utilized a low-cost technique to diagnose Candidemia in these patients but were limited by lack of further confirmatory testing. The growing incidence of Candidemia can be curbed by frequent changes in intravenous lines, targeted investigations for at-risk preterms including those undergoing gastrointestinal surgeries and limiting use of broad-spectrum antibiotics while adhering to recommended durations of antimicrobial therapy and discontinuing at the earliest opportunity.

The incidence, speciation and resistance profile of hospital-acquired candidemia at the Tikur Anbessa Specialized teaching hospital should be further analyzed. The need for such a study is particularly important in light of its contribution in preventing the unjustified use of parenteral antibiotics in early life sepsis without a confirmed bacterial etiology leading to multi-drug resistant hospital pathogens.

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Competing interest

The authors declare that this manuscript was approved by all authors in its form and that no competing interest exists.

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PERSPECTIVE

NEONATAL AND CHILDHOOD EYE HEALTH: NEED FOR IMMEDIATE/ INNOVATIVE CHANGE IN ETHIOPIA

Sadik Taju Sherief, MD[1*], Wondu Alemayehu, MD, MPH[2] , Aida Abashawl MD,MPH[2]

As in many low and middle-income countries, child eye health is a significant public health problem in Ethiopia; a country in which children under 15 years of age constitute about 50% of its population. It is a known fact that the causes of childhood blindness and visual impairment are different from adults and many are preventable at community level, and blinding conditions can also increase child mortality. Loss of vision can have huge repercussions on a child's quality of life. Surviving children are subjected to large numbers of “blind years” and/or lazy eye (amblyopia) that "shuts off" with permanent loss of vision if not identified early and get treated. (1).

Globally, 19 million children, are estimated to be visually impaired. (2). Approximately 75% of blind children live in low-income countries. Almost half of blindness and low vision in LICs is due to avoidable causes such as corneal scarring from measles infection, vitamin A deficiency disorders, use of harmful traditional eye remedies, ophthalmia neonatorum and cataract (3)

According to the national survey of blindness and low vision, of 2006, the prevalence of childhood blindness is 0.1% accounting for over 6% of the total blindness burden in Ethiopia. (4) A cross-sectional population-based survey in Southwest Ethiopia revealed lens related abnormalities (mainly congenital Cataract) were the leading causes of blindness. (5) A hospital based cross-sectional study of childhood ocular morbidity showed conjunctivitis, ocular trauma and refractive errors were the most common conditions encountered (6)

Regarding the huge problem of uncorrected refractive error (URE); farsightedness can lead to strabismus (squinting), such as crossed eyes, for which surgery may be required. Untreated strabismus can lead to amblyopia and/or lazy eye. Nearsightedness, also called myopia, can be completely corrected with glasses in most cases. Astigmatism often causes blurred or distorted vision at all distances. Like nearsightedness and farsightedness, astigmatism can be corrected with glasses. (6-8)

Childhood blindness is a significant contributor to the the global economic burden of blindness and disability-adjusted life years. Good primary health care and personnel trained in primary eye care are essential for the control of blindness in children (9). Trained human power is the key to control avoidable childhood blindness and low vison. Shortage of skilled trained manpower in the field of pediatrics and strabismus Ophthalmology is the bottleneck for child eye health in Ethiopia.

Robust plans to work in collaboration with the MOH, MOE’s universities’ departments of Ophthalmology and pediatrics, and other stakeholders should be developed and implemented. These activities would include training of pediatricians, residents, nursing staff as well as health professionals at health facilities in rural and urban settings. Early detection and prompt treatment and/or referral of neonates with Retinopathy of Prematurity and children with ocular disorders, at base and rural outreach sites, are essential to avoid lifelong visual impairment. Establishment of centers and strengthening a referral system between pediatric and ophthalmology services is highly critical.

Data gathering, analysis and reporting must be a key focus in order to generate information on common eye diseases and examine the challenges and opportunities in integrating eye health in general health/pediatric care. Curriculum and policy development at Ministries of Health and Education; Universities and Faculties; professional societies such as the Ophthalmological Society of Ethiopia and Association of Pediatricians is of paramount importance.

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EDITORIAL POLICY

Overview

Ethiopia's oldest medical journal, *The Ethiopian Medical Journal (EMJ)* is the official organ of the Ethiopian Medical Association (EMA). The EMJ is devoted to the advancement and dissemination of knowledge pertaining to the broad field of medicine in Ethiopia and other developing countries. The journal first appeared in July 1962 and has been published quarterly (January, April, July, October) without fail since then. It has been published in both online (www.emjema.org) and hard copy (ISSN0014-1755) versions.

The EMJ continues to play an important role in documenting and disseminating the progress of scientific medicine, and in providing evidence base for health policy and clinical practice in Ethiopia and Africa at large.

Our online journal is open access. The hard copies are distributed to members of the Ethiopian Medical Association. Hard copies of the Journal are distributed to institutions and organizations (internal and external) based on subscription.

Reviewing procedure

Peer reviewers

The Ethiopian Medical Journal uses a double-blind review system for all manuscripts. Each manuscript is reviewed by at least two reviewers. The reviewers act independently, and they are not aware of each other's identities. The reviewers are selected solely based on their relevant expertise for evaluating a manuscript. They must not be from the same institution as the author(s) of the manuscript, nor be their co-authors in the recent past. The purpose of peer review is to assist the author in improving papers and the Editorial Board in making decision on whether to accept or reject a manuscript. Reviewers are requested to decline if they have a conflict of interest or if the work does not fall within their expertise.

Peer review process

Manuscripts are sent for review only if they pass the initial evaluation (pre-review by the Editorial Board) regarding their style, methodological accuracy, ethical review documentation and thematic scope. A special care is taken that the initial (pre-review) evaluation is done in 3-5 days.

The Journal policy is to minimize time from submission to publication without reducing peer review quality. Currently the total period from the submission of a manuscript until its publication takes an average of six months. Peer reviewers are requested to respond within four weeks. During the review process, the Editor-in-Chief may require authors to provide additional information (including raw data) if they are necessary for the evaluation of the manuscript. These materials shall be kept confidential and must not be used for any other purposes.

The entire review process takes place under the supervision of the Editor-in-Chief in an online environment, with the assistance of the Journal Secretariat. The online system also allows authors to track the manuscript review progress.

Resolving inconsistencies

In case that the authors have serious and reasonable objections to the reviews, the Editorial Board assesses whether a review is objective and whether it meets academic standards. If there is a doubt about the objectivity or quality of review, the Editor-in-Chief will assign additional reviewer(s).

Additional reviewers may also be assigned when reviewers' decisions (accept or reject) are contrary to each other or otherwise substantially incompatible. The final decision on the acceptance of the manuscript for publication rests solely with the Editor-in-Chief.

Responsibilities

Authors' responsibilities

This is provided in the '*Guidelines to Authors'* which appear in each issue of the Journal. Authors must guarantee that their manuscripts are their original work, that they have not been published before, and are not under consideration for publication elsewhere. Parallel submission of the same paper to another journal constitutes misconduct and eliminates the manuscript from further consideration. Work that has already been published elsewhere cannot be reprinted in the Ethiopian Medical Journal

Authors are exclusively responsible for the contents of their submissions and must make sure that the authors listed in the manuscript include all and only those authors who have significantly contributed to the submitted manuscript. If persons other than authors were involved in important aspects of the research project and the preparation of the manuscript, their contribution should be acknowledged in the Acknowledgments section.

It is the responsibility of the authors to specify the title and code label of the research project within which the work was created, as well as the full title of the funding institution. In case a submitted manuscript has been presented at a conference in the form of an oral presentation (under the same or similar title), detailed information about what was published in proceedings of the conference shall be provided to the Editor-in-Chief upon submission.

Authors are required to properly cite sources that have significantly influenced their research and their manuscript. Parts of the manuscript, including text, equations, pictures, tables and graphs that are taken verbatim from other works must be clearly marked, e.g. by quotation marks accompanied by their location in the original document (page number), or, if more extensive, given in a separate paragraph.

Full references of each quotation (in-text citation) must be listed in the separate reference section in a uniform manner, according to the citation style used by the journal. References section should list only quoted/cited, and not all sources used for the preparation of a manuscript.

When authors discover a significant error or inaccuracy in their own published work, it is their obligation to promptly notify the Editor-in-Chief and cooperate with him/her to retract or correct the paper.

Authors should disclose in their manuscript any financial or other substantive conflict of interest that might have influenced the presented results or their interpretation.

By submitting a manuscript, the authors agree to abide by the Editorial Policies of the Ethiopian Medical Journal

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Editorial responsibilities

The Editor-in-Chief is responsible for deciding which articles submitted to the journal will be published. The decisions are made based exclusively on the manuscript's merit. They must be free from any racial, gender, sexual, religious, ethnic, or political bias. When making decisions the Editor-in-Chief is also guided by the editorial policy and legal provisions relating to defamation, copyright infringement and plagiarism.

Members of the Editorial Board including the Editor-in-Chief must hold no conflict of interest about the articles they consider for publication. Members who feel they might be perceived as being involved in such a conflict do not participate in the decision process for a manuscript.

The information and ideas presented in submitted manuscripts shall be kept confidential.

Editors and the editorial staff shall take all reasonable measures to ensure that the authors/reviewers remain anonymous during and after the evaluation process in accordance with the type of reviewing in use.

The Editorial Board is obliged to assist reviewers with additional information on the manuscript, including the results of checking manuscript for plagiarism.

Reviewers' responsibilities

Reviewers are required to provide the qualified and timely assessment of the scholarly merits of the manuscript. The reviewer takes special care of the real contribution and originality of the manuscript. The review must be fully objective, and the judgment of the reviewers must be clear and substantiated by arguments.

The reviewers assess manuscript for the compliance with the profile of the journal, the relevance of the investigated topic and applied methods, the scientific relevance of information presented in the manuscript, and the pres-

entation style. The review has a standard format. It is submitted through the online journal management system where it is stored permanently.
The reviewer must not be in a conflict of interest with the authors or funders of research. If such a conflict exists, the reviewer is obliged to promptly notify the Editor-in-Chief. The reviewer shall not accept for reviewing papers beyond the field of his/her full competence.
Reviewers should alert the Editor-in-Chief to any well-founded suspicions or the knowledge of possible violations of ethical standards by the authors. Reviewers should recognize relevant published works that have not been considered in the manuscript. They may recommend specific references for citation but shall not require citing papers published in the Ethiopian Medical Journal, or their own papers, unless it is justified.
The reviewers are expected to improve the quality of the manuscript through their suggestions. If they recommend correction of the manuscript prior to publication, they are obliged to specify the way this can be achieved. Any manuscript received for review must be treated as confidential document.

Ethical Considerations
Dealing with unethical behavior
Anyone may inform the Editor-in-Chief at any time of suspected unethical behavior or any type of misconduct by giving the necessary credible information/evidence to start an investigation.

- Editor-in-Chief makes the decision regarding the initiation of an investigation.
- During an investigation, any evidence should be treated as confidential and only made available to those strictly involved in the process.
- The accused will always be given the chance to respond to any charges made against them.

If it is judged at the end of the investigation that misconduct has occurred, then it will be classified as either minor or serious.

Minor misconduct (with no influence on the integrity of the paper and the journal, for example, when it comes to misunderstanding or wrong application of publishing standards) will be dealt with directly with authors and reviewers without involving any other parties. Outcomes include:

- Sending a warning letter to authors and/or reviewers.
- Publishing correction of a paper, e.g. when sources properly quoted in the text are omitted from the reference list.

Publishing an erratum, e.g. if the error was made by editorial staff.

In the case of major misconduct, the Editor-in-Chief may adopt different measures:

- Publication of a formal announcement or editorial describing the misconduct.
- Informing officially the author's/reviewer's affiliating institution.

The formal, announced retraction of publications from the journal in accordance with the Retraction Policy.

- A ban on submissions from an individual for a defined period.

Referring a case to a professional organization or legal authority for further investigation and action.

The above actions may be taken separately or jointly. If necessary, in the process of resolving the case relevant expert organizations, bodies, or individuals may be consulted.

When dealing with unethical behavior, the Editorial Board will rely on the guidelines and recommendations provided by the Committee on Publication Ethics (COPE).

Plagiarism prevention

The Ethiopian Medical Journal does not publish plagiarized papers. The Editorial Board has adopted the stance that plagiarism, where someone assumes another's ideas, words, or other creative expression as one's own, is a clear violation of scientific ethics. Plagiarism may also involve a violation of copyright law, punishable by legal action.

Plagiarism includes the following:

- Self-plagiarism, which is using one's own previous work in another context without citing that it was used previously
- Verbatim (word for word), or almost verbatim copying, or purposely paraphrasing portions of another author's work without clearly indicating the source or marking the copied fragment (for example, using quotation marks) in a way described under Authors' responsibilities;
- Copying equations, figures or tables from someone else's paper without properly citing the source and/or without permission from the original author or the copyright holder.

Any manuscript which shows obvious signs of plagiarism will be automatically rejected. In case plagiarism is discovered in a paper that has already been published by the journal, it will be retracted in accordance with the procedure described under Retraction policy, including blacklisting the author(s) .

To prevent plagiarism, the manuscripts are submitted to a plagiarism detection process. The results obtained are verified by the Editorial Board in accordance with the guidelines and recommendations of the Committee on Publication Ethics (COPE).

Retraction policy

Legal limitations of the publisher, copyright holder or author(s), infringements of professional ethical codes, such as multiple submissions, bogus claims of authorship, plagiarism, fraudulent use of data or any major misconduct require retraction of an article.

Occasionally, a retraction can be used to correct numerous serious errors, which cannot be covered by publishing corrections. A retraction may be published by the Editor-in-Chief, the author(s), or both parties consensually.

The retraction takes the form of a separate item listed in the contents and labeled as "Retraction".
The original article is retained unchanged, except for a watermark on the PDF indicating on each page that it is "retracted".

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Open access policy

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Article processing charge

The Ethiopian Medical Journal does not charge authors or any third party for publication in its regular quarterly Issues. Both manuscript submission and processing services, and article publishing services are free of charge.
There are no hidden costs whatsoever.

GUIDELINES FOR AUTHORS

The *Ethiopian Medical Journal (EMJ)* is the official Journal of the Ethiopian Medical Association (EMA) devoted to the advancement and dissemination of knowledge pertaining to the broad field of medicine in Ethiopia and other developing countries. Prospective contributors to the Journal should take note of the instructions of Manuscript preparation and submission to EMJ as outlined below.

Article types acceptable by EMJ

Original Articles (*vide infra*) on experimental and observational studies with clinical relevance
Brief Communications
Case Series
Case Reports
Editorials, Review or Teaching Articles: by invitation of the Editorial Board.
Correspondences/Letters to the Editor
Monographs or set of articles on specific themes appearing in a Special Issues of the Journal
Book reviews
Perspectives,
Viewpoints
Hypothesis or discussion of an issue important to medical practice
Letter to the Editor
Commentaries
Advertisements
Obituaries

N.B. Articles are not acceptable if previously published or submitted elsewhere in print or electronic format, except in the form of abstracts in proceedings of conferences.

Content and format of articles:

Title: The title should be on a separate page. It should not have acronyms or abbreviations. The title should be descriptive and should `not exceed 20 words or 120 characters including space. The title page should include the name(s) and qualification of the author(s); the department or Institution to which the study/research is attributed and address of the corresponding Author. If the author has multiple affiliations only use the most preferred one.

1. Original Articles

2,500 words, excluding Abstracts, References, Figures and Tables. The manuscript of the Article, should appear under the following headings:

a) Abstract: The abstract of the Article is prepared on a separate paper, a maximum of 250 words; it should be structured under the titles: a) Background; b) Methods; c) Results; d) Conclusions. Briefly summarize the essential features of the article under above headings, respectively. Mention the problem being addressed in the study; how the study was conducted; the results and what the author(s) concluded from the results. Statistical method used can appear under Methods paragraph of the Abstract, but do not insert abbreviations or references in the Abstract section.

Keywords: Provide three to six key words, or short phrases at the end of abstract page. Use terms from medical subject heading of Index Medicus to assist in cross indexing the Article.

b) Introduction : Should provide a short background and context of the study and provide the rationale for doing the study. It should not be a detailed review of the subject and should not include conclusions from the paper.

c) **Patients or (Materials) and Methods:** should contain details to enable reproducibility of the study by others. This section must include a clear statement specifying that a free and informed consent of the subjects or their legal guardians was obtained. Corresponding author should submit a copy of institution review Board (IRB) clearance or letter of permission from the hospital or department (if IRB exempt) with the manuscript. For manuscripts on clinical trials, a copy of ethical approval letter from the concerned body should be submitted with the Manuscript. If confidential data is being used for publication (such as student grades, medical board data, or federal ethics board data), then appropriate support/ agreement letter should be included. Photos of patients should disguise the identity or must have obtained their written consent. Reference number for ethical approval given by ethics committee should be stated. In general, the section should include only information that was available at the time the plan or protocol for the study was being written; all information obtained during the study belongs in the Results section.

d) **Results:** This section should present the experimental or observational data in text, tables or figures. The data in Tables and Figures should not be described extensively in the text.

e) **Discussion:** The first paragraph should provide a summary of key finding that will then be discussed one by one in the paragraphs to follow. The discussion should focus on the interpretation and significance of the results of the study with comments that compare and describe their relation to the work of others (with references) to the topic. Do not repeat information of Results in this section. Make sure the limitations of the study are clearly stated.

f) **Tables and Figures:** These should not be more than six. Tables should be typed in triplicate on separate sheets and given serial Arabic numbers. Titles should be clearly place underneath Tables and above Figures. Unnecessary and lengthy tables and figures are discouraged. Same results should not be presented in more than one form (choose either figure or table). Units should appear in parentheses in captions but not in the body of the table. Statistical procedures, if not in common use, should be detailed in the METHODS section or supported by references. Legends for figures should be typed on separate sheets, not stapled to the figures. Three dimensional histograms are discouraged. Recognizable photographs of patients should be disguised. Authors should submit editable soft versions of the tables and figures.

g) **Acknowledgement:** Appropriate recognition of contributors to the research, not included under Authors should be mentioned here; also add a note about source of the financial support or research funding, when applicable.

h) **References**:

- The titles of journals should be abbreviated according to the style used for MEDLINE (www.ncbi.nlm.nih.gov/nlmcatalog/journals).
- References should be numbered consecutively in the order in which they are first mentioned in the text and identify references in text, tables, and legends by Arabic numerals in parentheses.
- Type the References on a separate sheet, double spaced and keyed to the text.
- Personal communications should be placed NOT in the list of references but in the text in parentheses, giving name, date and place where the information was gathered or the work carried out (e.g. personal communication, Alasebu Berhanu, MD, 1984, Gondar College of Medical Sciences). Unpublished data should also be referred to in the text.
- References with six or less authors should all be listed. If more than six names, list the first three, followed by et al.
- Listing of a reference to a journal should be according to the guidelines of the International Committee of Medical Journal Editors ("Vancouver Style') and should include authors' name(s) and initial(s) separated by commas, full title of the article, correctly abbreviated name of the journal, year, volume number and first and last page numbers.
- Reference to a book should contain author's or authors' name(s) and initials, title of chapter, names of editors, title or book, city and name of publisher, year, first and last page numbers.

The following examples demonstrate the acceptable reference styles.

Articles:

- Gilbert C, Foster A. Childhood blindness in the context of Vision 2020: the right to sight. *Bull World Health Org 2001;79:227-32*
- Teklu B. Disease patterns amongst civil servants in Addis Ababa: an analysis of outpatient visits to a Bank employee's clinic. *Ethiop Med J 1980;18:1-6*
- Tsega E, Mengesha B, Nordenfelt E, Hansen B-G; Lindberg J. Serological survey of human immuno-deficiency virus infection in Ethiopia. *Ethiop Med J 1988; 26(4): 179-84*
- Laird M, Deen M, Brooks S, et al. Telemedicine diagnosis of diabetic retinopathy and glaucoma by direct ophthalmoscopy (Abstract). *Invest Ophthalmol Vis Sci 1996; 37:104-5*

Books and chapters from books:

- Henderson JW. Orbital Tumors, 3rd ed. Raven Press New York, 1994. Pp 125-136.
- Clipard JP. Dry Eye disorders. In Albert DM, Jakobiec FA (Eds). Principles and Practice of Ophthal-mology. W.B Saunders: Philadelphia, PA 1994 pp257-76.

Website:

- David K Lynch; laser History: Masers and lasers. http://home.achilles.net/jtalbot/history/massers.htmAccessed 19/04/2001

2. **Brief Communication**

Short versions of Research and Applications articles, often describing focused approaches to solve a health problem, or prelnary evaluation of a novel system or methodology

- Word count: up to 2000 words
- Abstract up to 200 words; excluding: Abstract, Title, Tables/Figures and References
- Tables and Figures up to 5
- References (vide supra – Original Article)

3. **Case Series**

Minimum of three and maximum of 20 cases

- Up to 1,000 words; excluding: Abstract, Title, Tables/Figures and References
- Abstract of up to 200 words; structured; (vide supra)
- Statistical statements here are expressed as 5/8 (62.5%)
- Tables and Figures: no more than three
- References: maximum of 20

4. **Case Report**

Report on a rare case or uncommon manifestation of a disease of academic or practical significance

- Up to 750 words; excluding: Abstract, Title, Tables/Figures and References
- Abstract of up to 100 words; unstructured;
- Tables and Figures: no more than three
- References: maximum of 10

5. **Systematic review**

Review of the literature on topics of broad scientific interest and relevant to EMJ readers

- Abstract structured with headings as for an Original Article (*vide supra*)
- Text should follow the same format as what is required of an Original Article
- Word count: up to 8,000 words, excluding abstract, tables/Figures and references
- Structured abstract up to 250 words
- Tables and Figures up to 8

6. **Teaching Article**

A comprehensive treatise of a specific topic/subject, considered as relevant to clinical medicine and public health targeting EMJ readers

- By invitation of the Editorial Board; but an outline of proposal can be submitted
- Word limit of 8,000; excluding abstract, tables/Figures and references
- Unstructured Abstract up to 250 words

7. Editorial

- By invitation of the Editorial Board, but an editorial topic can be proposed and submitted
- Word limit of 1,000 words: excluding references and title; no Abstract
- References up to 15.

8. Perspectives

- By invitation of the Editorial board, but a topic can be proposed and submitted
- Word limit of 1,500
- References up to six

9. Obituaries

- By invitation of the Editorial board, but readers are welcome to suggest individuals (members of the EMA) to be featured.

Preparation of manuscripts

- Manuscripts must be prepared in English, the official language of the Journal.
- On a single separate sheet, there must be the title of the paper, with key words for indexing if required, and each author's full name and professional degrees, department where work was done, present address of any author if different from that where work was done, the name and full mailing address of the corresponding author, including email, and word count of the manuscript (excluding title page, abstract, references, figures and tables). Each table/figures/boxes or other illustrations, complete with title and footnotes, should be on a separate page.
- All pages should be numbered consecutively in the following order: Title page; Abstract and keywords page; main manuscript text pages; References pages; acknowledgment page; Figure-legends and Tables
- The Metric system of weights and measures must be used; temperature is indicated in degrees Centigrade.
- Generic names should be used for drugs, followed by propriety brand name; the manufacturer name in parenthesis, e.g. diazepam (Valium, Roche UK)
- Statistical estimates e.g. mean, median proportions and percentages should be given to one decimal place; standard deviations, odds ratios or relative risks and confidence intervals to two decimal places.
- Acronyms/Abbreviations should be used sparingly and must be given in full, at first mention in the text and at the head of Tables/foot of Figure, if used in tables/figures.eg. Blood Urea Nitrogen (BUN). Interstitial lung disease (ILD).
- Use the binomial nomenclature, reference to a bacterium must be given in full and underlined - underlining in typescript becomes italics in print (e.g. *Hemophilus influenzae)*, and later reference may show a capitalised initial for the genus (e.g. *H. influenzae)*
- In the text of an article, the first reference to any medical phrase must be given in full, with the initials following in parentheses, e.g., blood urea nitrogen (BUN); in later references, the initials may be used.
- Manuscripts for submission should be prepared in Microsoft Word document file format

Submission of manuscripts

- As part of the submission process, authors are required to check off their submission's compliance with journals requirements

- All manuscripts must be submitted to the Editor-in-Chief of the Journal with a statement signed by each author that the paper has not been published elsewhere in whole or in part and is not submitted elsewhere while offered to the *Ethiopian Medical Journal*. This does not refer to abstracts of oral communications at conferences/symposia or other proceedings.
- It is the author's responsibility to proof-read the typescript or off-print before submitting or re-submitting it to the Journal, and to ensure that the spelling and numerals in the text and tables are accurate.
- Authors should submit their work through the Ethiopian Medical Journal website; ema.emj@telecom.net.et.

Conflict of interest

Authors should disclose at the time of submission of manuscripts any conflict of interest, which refers to situations in which financial or other personal considerations may compromise, or have the appearance of compromising their professional judgment in conducting or reporting the research results They should declare that there is no conflict of interest to declare if there is none,

Manuscripts review procedures

The procedures for manuscripts review include:

- Within one week of receipt of a manuscript, the Editorial Board will review it in reference to (i) conformity with the Journal's "guidelines to authors (revised version available in all issues starting January 2020)", (ii) relevance of the article to the objectives of the *EMJ*, (iii) clarity of presentation, and (iv) plagiarism by using appropriate software
- The Editorial Board has three options: accept manuscripts for external review, return it to author for revision, or reject it. A manuscript not accepted by a board member is blindly reviewed by another board member. If not accepted by both, the manuscript is rejected by the Editorial Board. Decision will be made by the suggestion of a third Editorial Board member if the decisions of first two do not concur.
- Once accepted for external review, the Editorial Board identifies one (for brief communication, case reports, and teaching articles) or two (for original articles) reviewers with appropriate expertise. The reviewers will be asked to review and return manuscripts with their comments online within two weeks of their receipt. Reviewers have four options; accept, accept with major revision, accept with minor revision, or reject.
- A Manuscript accepted subject revision as suggested by reviewers will be returned to the corresponding author. Author(s) will be given four weeks to respond to reviewers' comments, make necessary changes, and return the manuscript to the Editorial Board. A Manuscript not returned within the specified time will be considered withdrawn by the author(s).
- Manuscripts with minor revisions will be cleared by the Editorial Board and accepted for publication. Those with major revisions will be returned to external reviewers and follow the procedures as outlined for the initial review.

General information

The Editorial Board reserves the right for final acceptance, rejection or editorial correction of papers submitted. However, authors are encouraged to write an appeal to the Editor-in-Chief for reconsideration of rejected manuscripts or any other complaints they might have.

Accepted papers are subject to Editorial revision as required and become the copy-right of the EMA Twenty-five reprints of published articles are supplied free to the first/corresponding author.

The Editorial Board welcomes comments on the guidelines from Journal readers.

Privacy statement

The names and email addresses entered in this journal site will be used exclusively for the stated purposes of this journal and will not be made available for any other purpose or to any other party.

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THE ETHIOPIAN MEDICAL JOURNAL

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If you are a paid–up member of EMA, and have not received your copy of EMJ, please notify the secretary, with the support of your ID card or letter from your hospital. Also, if you are transferred to a different hospital or institution, please return the following change of address form **PROMPTLY.**

NAME (in block) .....……...
FORMER ADDRESS: .....……..
P. O. BOX ..... CITY/TOWN .....
NEW ADDRESS .....……
INSTITUTION .....……
P. O. BOX ..... CITY/TOWN .....….