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EDITORIAL

ORIGINAL ARTICLES

CASE SERIES

CASE REPORT

Tsinuel Girma, Mirkuzie Woldie. *Ethiop Med J, 2021, Vol. 59, No. 3*

EDITORIAL

CLINICIANS ARE CRITICAL IN THE SENSEMAKING AND CO-PRODUCTION OF HIGH-QUALITY SERVICES

Tsinuel Girma, MD, PhD[1*], Mirkuzie Woldie, MD, MPH[1, 2]

Delivering consistently high-quality services is often challenging as the health care system is complex, embedded in, and affected by other even more complex systems. In low and middle-income countries, low-quality health care costs millions of lives each year (1, 2). Most health facilities suffer from poor infrastructure, inadequate supply of essential drugs, and equipment. More importantly, however, issues related to competence and engagement of front-line care providers (clinicians) are critical. Strategies and interventions that improve clinicians' sensemaking and engagement bring effective, efficient, and safety clinical care.

The biggest challenge globally in addressing the growing implementation gap in providing high-quality care is ineffective engagement and inauthentic partnering with clinicians. Health managers usually design quality and safety strategies and interventions in a top-down approach, without consultation and input from local clinicians (3). Clinicians are disregarded despite their central role in health care delivery and insider's knowledge and wisdom. The practical and conjectural knowledge they have are essential mixes of reasoning (complex, tacit, and hard to share) to develop and implement quality improvement interventions that are contextual (4). Gaining a deeper understanding of contexts makes developing effective and practical quality improvement projects is easier (5).

Clinicians of every discipline and at every level should continuously work on sensemaking - a diagnostic process directed at constructing plausible interpretations and understanding complex situations, enabling purposeful action. Clinicians can make sense of their organization, but also in the context of delivering care to individuals (6). For instance, observing how clinical teams rounded on their patients would reflect their assessment and task prioritization. Also, a look at how they recognize, assess, and make sense of medical complications gives insight into the practice of sensemaking.

Effective provider sensemaking is one path to achieving high-quality health care. In Ethiopia, clinicians perform several small-scale successful quality improvement projects based on real-life challenges within their facilities. Clinicians take the lead in these collaborative work that involve several members from different departments, including administrative staff. Ensuring quality is a collaborative effort and requires making sense of things with the help of local data that ultimately supports decision-making. Effective sensemaking also requires prospective or retrospective data. In the process of care, providers generate a large amount of data. However, these data are not utilized to evaluate the quality of care, explain challenges or develop evidence-informed context-specific innovations. The clinician should therefore strive to not only generate quality data but also use data for quality (5).

It is high time that clinicians are given a central role in improving the quality of care and share their learnings with the wider medical community. In this respect, health system managers at all levels should recognize the indispensable and critical role of the clinician in the co-production of quality care. They must use existing platforms and other innovative approaches to tap into this vast potential. At the same time, clinicians should value their strategic and critical role in achieving quality and thus use every opportunity for meaningful engagement to mitigate avoidable deaths and deliver safe and quality clinical care.

Through these engagements, clinicians will further develop critical thinking and problem solving skills helpful in properly positioning themselves in the complex situations of a complex system. Moreover, sensemaking of complex situations and organizations synergizes and boosts clinical reasoning - how clinicians understand patients – as a result of which quality of care and outcome improves. They will also make sense of the competing tasks that require problem prioritization and resource allocation.

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In order to achieve effective co-production of high-quality care, clinicians must have perspectives with high resolution and clarity like an eagle. However, to avoid being locked in with a narrow view, they also require a dragonfly-like perspective (360 degrees and multi-color) of being oriented to the context they operate in.

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OUALI Siheme, ZEMRI Khalida, Sellam Feriel, HARIR Noria, BENAISSA Zahira, HEBRI Sid Tadj, BENSABER Ouassini, NADJI Zouaoui, ELMEHADJI Dounia Zad. *Ethiop Med J, 2021, Vol. 59, No. 3*

ORIGINAL ARTICLE

CLINICAL CHARACTERISTICS OF RHEUMATOID ARTHRITIS IN WESTERN ALGERIA: A SINGLE CENTER EXPERIENCE

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ABSTRACT

Introduction: *Rheumatoid arthritis (RA) is the most common inflammatory rheumatic disease of multifactorial origin in adults and chronic autoimmune disease with a prevalence of 0.5% in the world. The aim of this study was to determine the clinical characteristics, therapeutic parameters and estimating the impact of smoking on disease onset of RA characteristics in Western Algerian region (Sidi bel Abbes area in particular).*

Methods: *A retrospective study was carried out on medical records of 300 patients with RA diagnosed (between 2015-2019) in the internal medicine department of the University Hospital of Sidi Bel Abbes region.*

Results: *Out of all the enrolled participants in this study, 257 (85.7 %) were females and 43(14.3%) were males. The mean age at diagnosis was 52.71±12.22, ranging from 14 to 84 years old. The average time of disease duration was 4.17±3.93 years. moderate activity was noted in 53.7% of subjects. The main medical histories were high blood pressure (41%), type 2 diabetes (84.7%), hypothyroiditis (6 %) and osteoporosis (4.7%). The majority of patients (81.3%) were seropositive and used DAMRDS (Disease Modifying Anti-Rheumatic Drug) as treatment. Moreover, evidence of association between smoking and ACPA was noticed with p=0.001, and most of the smokers were hypertensive (p =* ***0.0001)*** *and suffered from Hashimoto's thyroiditis (****p<0.0001).***

Conclusion: *This study showed that relatively older adults were commonly affected; the majority were seropositive and diagnosed in moderate stage of the disease. Smoking increased the risk of ACPA(anti-citrullinated protein antibodies) secretion and the emergence of comorbid diseases.*

Keywords: *Rheumatoid Arthritis Patients; Clinical Characteristics; Treatment; Smoking; Western Algeria Region.*

INTRODUCTION

Rheumatoid arthritis (RA) is the most common inflammatory rheumatic disease in adults(1). It is characterized by bilateral and symmetrical synovitis of appendicular skeleton joints and upper cervical spine. It affects very little the antheses, unlike spondyloarthritis, and it usually starts at the hand, wrist and forefoot(2). It is considered as an autoimmune disease because of the presence of rheumatoid factors (RF) and Anti Citrullinated Peptides Antibodies (ACPA) (3). Clinical and biological features of the disease vary according to the geographical location which could be explained by life style and cultural differences(4). The prevalence of RA is 0.5% worldwide and it varies from country to country (5). However the pathology is mostly common among the age groups of 35 to 55 years, and it is four times more frequent in women than men(6).

In Algeria the number of rheumatologists is modest compared to African countries. However, the difficulty of access to biological treatment is a main problem due to their availability only at university hospitals (4). Moreover, the major survey conducted in Algeria from February 14th to April 11th, 2013, identified over 100,000 cases of Rheumatoid arthritis RA (7).

The associations of smoking and genetic factors were incriminated in the development and the severity of RA (8–11). Interestingly, previous studies have underlined the impact of smoking on RA outcomes such as disease activity, radiologic damages, positive ACPA(8)

Thus, the aim of this study was to describe clinical characteristics of patients with rheumatoid arthritis in the Western Algerian region and the impact of smoking on RA outcomes.

PATIENTS AND METHODS

Population

This hospital-based study was carried out at the internal medicine department of the University Hospital of Sidi-bel- Abbes region from January 2015 to April 2019.

We carried out a retrospective epidemiological study using records of 300 patients' with RA diagnosed according to the ACR 1987 criteria. The following variables were considered as factors: age at onset, gender, disease duration, joint disorders, DAS28 (Disease activity score 28), comorbidities, biological assessment, treatments, and smoking at disease onset.

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A comparative study between smokers and non-smokers RA patients was performed.
Concerning DAS28, the threshold values are less than 2.6 for remission, from 2.6 to 3.2 for low activity, between 3.2 and 5 for moderate activity and over 5 for high activity(8).

The statistical analysis
Regarding the statistical analysis, the result was presented as frequencies with percentage and mean with standard deviation (SD). For comparison, continuous variables were tested using the independent sample t-test and Pearson chi-square test ($\chi 2$) was used for categorical variables. The level of significance was at p-vale <5%. All data were processed and analyzed using SPSS 22.0 (Statistical Package for the Social Sciences, IBM Corporation; Chicago, IL. August 2013).

Ethics: The Medical Committee of Sidi bel Abbes University Hospital and Department of Biology, Djillali Liabes University approved the study.

RESULTS

Demographic, clinical characteristics and medication related information
Three hundred (300) cases were enrolled in this study between 2015-2019 with 257 (85.7 %) females and 43 (14.3%) males). A clear female predominance was noticed with the female to male ratio of 5.95, median age of the enrolled participants was 52.71±12.22, ranging from 14 to 84 years old. The most affected age group was the 56-60 years (19.7%).

More cases were from urban areas (72.7%) than rural area (27.3%). The average disease duration was 4.17±3.93.

The most reported joint disorders were on hands (68.3%) followed by wrists (62.3%), knees (55.7%), elbows (37.3%), shoulders (35%),feet (31%), and ankle (14.7%). 15.7% of patients had erosive rheumatoid arthritis.

After the classification according to the disease activity score 28 (DAS28), we noticed a predominance of moderate activity (53.7%), followed by high disease activity (32.3%), low activity (13%), and finally remission (1%).

The inflammatory and biological assessment showed that 198 (66%) of patients had a positive CRP (C reactive protein), 247(82.3%) had an accelerated Erythrocyte Sedimentation Rate (ESR) and 64(23.1%) had anemia.

Among the included patients, 244(81.3%) were seropositive for RF(Rheumatoid Factors) and 242 (80.7%) were seropositive for ACPA. Only 5.7% were demonstrated infected with Escherichia coli (Table 1).

The most recorded medical histories were: menopause (45.5% of females) followed by high blood pressure (41%), type 2 diabetes (15.3%), Hypothyroiditis (6%), and osteoporosis (4.7%) (Table 2).

Leflunomide was the most commonly used DMARD followed by Methotrexate, *Glucocorticoid*, non-steroidal anti-inflammatory drugs, Sulfasalazine and Hydroxychloroquine. 80 (26.7%) of patients were treated by biotherapy, the most used was tocilizumab (11.3%) (Table 3).

Smoking Status:
According to the findings, 9% were smokers (P<0.0001).Smokers did not differ in age, radiologic progression and DAS28 comparing to non -smoker patients. However, a significant relation was found between smoker group and ACPA titer (p=0.001) but not with RF and ESR(Table 4).
With regards to comorbidities, the study revealed that, majority of smokers suffered from high blood pressure (p = **0.0001)** and Hashimoto's thyroiditis **(p<0.0001).** Moreover**,** 3 smokers patients suffered from Pulmonary fibrosis (**P=0.0001**) (Table 5).

Table 5: The comorbidities profile of RA smoking patients

Comorbidities	Smoker	Non-Smoker	Pvalue *
high blood pressure	21(7%)	102 (34%)	0.0001
Type 2 diabetes	2(0.7%)	44 (14.7%)	0.231
Hashimoto's thyroiditis	13 (4.3%)	5(1.7%)	<0.0001
Crohn disease	0	4(1.3%)	0.527
osteporosis	0	14(4.7%)	0.228
Pulmonary fibrosis	3(1%)	1(0.3%)	0.0001
Scleroderma	0	5(1.7%)	0.478
gastric ulcer	0	3(1%)	0.584
vitiligo	0	3(1%)	0.584
Anemia	4(1.3%)	60(20%)	0.386

* Pearson chi-square test ($\chi 2$)

Table 1: Characteristics of the RA patients

Characteristics	Rheumatoid arthritis n=300
Mean disease duration in years	4.17±3.93
Sex	
Female	257(85.7%)
Male	43(14.3%)
Age Years	52.71±12.22
14-30	14(4.7%)
31-36	19(6.3%)
37-42	29(9.7%)
43-48	39(13%)
49-54	54(18%)
55-60	59(19.7%)
61-66	52(17.3%)
67-72	27(9%)
73-78	5(1.7%)
79-84	2(0.7%)
Area of residence	
Rural	82(27.3%)
Urbain	218(72.7%)
The seat of joint damage	
Hands	205(68.3%)
Wrists	187(62.3%)
Knees	167(55.7%)
Elbows	112(37.3%)
Shoulders	105(35%)
Feets	93(31%)
Ankle	44(14.7%)
Erosion	47(15.7%)
Disease activity	
Remission	3(1%)
Low	39(13%)
Moderate	161(53.7%)
Hight	97(32.3%)
Anemia	64(21.3%)
Leukocytosis	21(7%)
Thrombocytosis	5(1.7%)
Leukopenia	9(3%)
Mean CRP titer (mg/l)	18.40±28.66
Positive CRP	198(66%)
Mean ESR titer (mm/h)	43.70±24.80
Accerelated ESR	247(82.3%)
Mean Rheumatoide factor titer (UI/ml)	70.40±75.73
Positive RF	244(81.3%)
Mean ACPA Titer (UI/ml)	195.49±167.09
Positive ACPA	242(80.7%)
Cytobacteriological examination of urine	
Escherichia coli	17(5.7%)

DAS28: disease activity score 28, CRP: C- reactive protein; ESR: Erythrocyte Sedimentation Rate RF: Rheumatoid Factors; ACPA : Anti Citrullinated Peptides Antibodies.Values are expressed as number (percentage) or mean ± standard deviation

Table 2 : The comorbidities profile of RA

Medical history	Number (%)
Menopause	117(45.5%)
high blood pressure	123(41%)
Type 2 diabetes	46(15.3%)
Hashimoto's thyroiditis	18(6%)
Crohn disease	4(1.3%)
Scleroderma	5(1.7%)
Sjogren	2(0.7%)
Psoriasis	1(0.3%)
osteopenia	4(1.3%)
osteporosis	14(4.7%)
Pulmonary fibrosis	4(1.3%)
Asthma	4(1.3%)
Tuberculosis	2(0.7%)
gastric ulcer	3(1%)
vitiligo	3(1%)
Tobbaco	27(9%)

Table 3: Medications RA Patients

Treatment	Number (%)
Leflunomide (Arava)	252(84%)
Methotrexate	244(81.3%)
Glucocorti-coid (Precortyl)	164(54.7%)
No Steroidal Anti-Inflammatory	112(37.3%)
Salazopyrine	14(4.7%)
Hydroxychloroquine (Plaquenil)	5(1.7%)
Glibil	4(1.3%)
Biotherapy	34(11.3%)
Tocilizumab	22(7.3%)
Adalimumab	9(3%)
infliximab	9(3%)
Etanercept	6(2%)
Rituximab	

Table 4: Characteristics of RA smoking patients

	Smoker	Non- Smoker	P value
Age	52.96±12.70	52.69±12.20	0.91[1]
Gender			
Female	0	257(85.7%)	<0.0001[2]
Male	27(9%)	16(5.3%)	
Erosion	8(2.7%)	66(22%)	0.53[2]
DAS28	4.58±1.08	4.53±1.22	0.83[1]
The seat of joint damage			
Hands	18(6%)	186(62%)	0.87[2]
Wrists	18(6%)	169(56.3%)	0.62[2]
Knees	16(5.3%)	151(50.3%)	0.96[2]
Elbows	12(4%)	100(33.3%)	0.42[2]
Shoulders	8(2.7%)	96(32%)	0.56[2]
Feets	9(3%)	84(28%)	0.78[2]
Ankle	6(2%)	38(12.7%)	0.24[2]
CRP	14.42±12.73	18.79±29.76	0.45[1]
ESR	41.48±25.63	43.92±24.75	0.62[1]
RF titer	79.13±50.56	69.53±77.79	0.53[1]
ACPA titer	296.04±159.95	185.55±164.74	0.001[1]

1 : the independent sample t- test

2: Pearson chi-square test ($\chi 2$)

DISCUSSION

To the best of our knowledge, the current study was the first one of its kind that studied the profile of rheumatoid arthritis in western Algeria in general and Sidi bel abbes region in particular, over a period of 4 years (2015-2019). This study aimed to describe the clinic-demographic profile of Rheumatoid Arthritis patients in western Algeria and examined the correlation between RA characteristics and smoking.

Rheumatoid arthritis is an autoimmune disease characterized by a feminine predominance (9,10), which is in agreement with our findings with a sex-ratio of 5.796 (female to male).

The mean age of patients at disease onset was 52,717±12,2273, and the most affected age group in our study was 56-60 years (19.7%). These data are comparable with those found by Slimani et al(4), who noticed that the most common age group was 41 and 60 years old with an average age of 50.10± 14.50. Moreover, the series of Machado-Alba et al(11), noted an average age of 53.2±13.9.

A sequence of joint damage was observed in the Andia et al series(12) in which these attacks started at the hand's (47.5%), followed by the wrist (18%), shoulders (11%), elbow (9.5%), ankle (6.5%), foot (5%) and knees (2%). Other study series of Ferreyra et al (13) showed different frequency of same joint damage. These results are comparable with those found in our series which showed a high frequency starting with hands followed by wrists, knees, elbows, shoulders, feet, and ankle.

The mean DAS28 (4.54±1.21) was very close to those reported in the series of Gülfe et al , Slimani et al at (4.3±1.4) (4,14), but different from other reports due to a late referral system (15,16).

CRP(C-Reactive Protein) seems to be the best test for measuring the acute phase of RA(17–19). Our study results indicated that 66% of patients had a positive CRP, which is in agreement with the findings of Humphreys et al (20) who showed that 48% of patients had a positive CRP. Brunier et al finding is also similar to our findings(21).

The combination of the two CRP and ESR biological tests provides information for a better diagnosis (21). The mean ESR was comparable with studies from Egypt (22) and Morocco (23).

RF and ACPA are important markers for the diagnosis of rheumatoid arthritis(24). Brunier et al (21) reported that 76.5% of patients had a positive RF and 66.7% had a positive ACPA, and 78.5 % had a positive RF.

In the survey of Ouali et al, 79.7% had a positive ACPA (25). Tantayakom et al revealed the presence of RF and ACPA among 70.4 and 72.4% patients respectively (15). According to our results, positive RF and ACPA was found in 81.3% and 80.7% of cases respectively.

56.8% of patients were postmenopausal in the findings of Lehlou et al (26). Similarly, the series of Ajlani et al(27) noted that 56.25% of women were menopausal. These results are comparable to our findings with a rate of 45.5%. This could be due to the decline in ovarian function (28,29).

Regarding comorbidities, the presence of hypertension in RA patients is reported to be significantly increased due to the oxidative stress (30). On the other hand insulin resistance was associated with increased levels of inflammatory mediators (interleukin 6; TNFα) in RA which explain the relationship between Type 2 diabetes and RA(31). Dougados et al (32) found that 40% of patients had hypertension, and 25% had type 2 diabetes (33). Jeong et al reported that 30.3% of cases had hypertension and 12.9% were diabetic. Our data indeed confirmed these results.

Many investigations showed the association between RA and osteoporosis mainly in premenopausal stage (34–36). According to our findings, 4.7% of patients suffered from osteoporosis. Furthermore, we found that 6.0% had Hypothyroiditis, scleroderma (1.7%), Crohn's disease (1.3%), Sjögren's syndrome (0.7%) and psoriasis (0.3%). These findings are also comparable with those of Machado et al (11) who showed that 10.2% of patients had other autoimmune diseases.

Methotrexate (MTX) and luflodamine were the most used treatments for RA (10). Similarly, Tantayakom et al (15) noted that MTX was prescribed in 88.4% of cases. Additionally, Machado-Alba et al (11) ensured the predominance of the MTX and luflodamine prescription. The current study also identified that, luflodamine (84.0%) and MTX (81.3%) were the most widely used classical background therapy.

Biotherapies are now part of therapeutic arsenal chronic inflammatory rheumatism such as rheumatoid arthritis (37). They differ from general public hospital to private hospital which explain the difficulty to access biological treatment (38). Slimani et al (4) stated that 4% of patients were treated with biotherapy and about 20% of patients were treated with biotherapy in the Machado-Alba et al series(11). With the current study, 26% had received a biotherapy.

Regarding the correlation of smoking status with some socio-demographic and clinical profile of RA patients, smoking was only associated with sex where more males smoke than females (P<0.0001). Similarly findings from the SCQM-RA registry in Switzerland reported that smokers were more often males. However, there are also other findings showing women as more smokers comparing to males(39,40). This is in contrast to our results.

Our findings demonstrated no difference in radiologic damages, disease activity, between smokers and non-smokers. These results are similar to Ruiz-Esquide et al, Finckh et al findings (39,41). But not replicated in other finding(42,43), which could be explained by the difference in the type of statistical analysis processed.

The increase risk of RA development and ACPA secretion were demonstrated associated with HLA-DRB1 genotype and smoking.
(44,45). Accordingly, a significant association between smoking and ACPA was observed (p=0.001) in the present study.

Smoking can have an impact on the development of associated comorbidities (46,47). Effectively, we noticed a significantly increased risk of Hyepretention, Hashimoto's thyroiditis, and pulmonary fibrosis among smoker group. Our results in line with several research studies; nevertheless, we worked over providing valuable information in order to establish the clinical, therapeutic features of the RA and the impact of smoking at disease onset in Western Algerian population. Besides, this study had several limitations; among which patients were evaluated according to AC R 1987 inclusion criteria.

In addition, the study is based on a single center with a small simple size, the lack of structural and functional quality assessment (SQA) of all patients, the insufficient information on average number of cigarettes smoked per day, duration of smoking, the lack of genetic testing in patients' files because of their cost.

Conclusion

In general, RA affected commonly older adults. The main reported joint disorders were on hands followed by wrists. Most of patients were seropositive and presented with moderate activity. Luflodamine and Methotrexate were the most commonly used treatments. Fewer patients were received biological treatment. Smoking at disease onset was associated with male gender, ACPA secretion and associated comorbidities such as hypertention and Hashimoto's thyroiditis.

For a better management of rheumatoid arthritis, more research on the impact of smoking on RA onset and severity are needed .

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ORIGINAL ARTICLE

ASSESSMENT OF THE SKILLS OF PAEDIATRIC RESIDENTS IN INTERPRETING EMERGENCY PAEDIATRIC RADIOGRAPHS

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ABSTRACT

Background*: Paediatrics Emergency ward is one of the critical wards in hospitals Overcrowding and the urgent nature of the patients make Emergency rooms a particularly challenging area. Therefore, fast and accurate diagnosis is very crucial & mandatory for proper patient management. So, Paediatrics residents, working in the Paediatric emergency section are required to have a basic interpretation of emergency radiographs for swift management. This study assessed the skill level of Paediatrics residents in interpreting emergency radiographs.*

Methods: *A Cross-sectional study was conducted among Paediatric residents in TikurAnbesa Specialized Hospital (TASH). Ten radiographs (7 Chest X-rays, 2 abdominal, and one extremity X-ray) were selected based on the most commonly seen emergency cases residents are expected to diagnose. The x-rays were displayed in PowerPoint and residents were asked to complete a questionnaire. A consultant radiologist also interpreted the images in the same setting. The data was then analyzed by using SPSS 25.0.*

Results: *A total of 79 Paediatrics residents were enrolled in this study. Only 32 (40.5 %)of the residents had a good skill level of interpretation with a 73% accuracy rate which was very low. The overall discrepancy rate was 49.6%. The sensitivity of the residents in detecting abnormal radiographs was 72 (91.1 %) with a specificity of 34 (43 %). A significant association was found with the year of residency*

Conclusions: S*kills of residents in interpreting radiographs were very low even if Paediatric emergency cases in the institution where this research was done constitute the largest proportion.*

Keywords: *Residents' skill, interpretation of x-rays, emergency patients. Ethiopia*

INTRODUCTION

Clinical decisions based on wrong interpretations have potential implications for patient care but there are situations where action must be taken immediately before formal verified reading is done by a radiologist. So, in most emergency departments immediate image interpretations are being done by non-radiology physicians. This is particularly important in identifying immediate life-threatening traumatic and non-traumatic emergencies. Even if there are reports of discrepancies between radiologists and primary care and emergency physicians, the rate of discrepancy is found to be variable.(1-3).

Imaging's are ordered and interpreted for immediate clinical decisions 24 hours a day by emergency physicians be it, Paediatrics residents, Paediatricians, or emergency physicians and the proper interpretation plays a key role in patient care(4).

Paediatric residents, as primary physicians at Paediatric ER, are required to preliminarily interpret emergency imaging & decide on the management of patients. Therefore, knowing the Paediatrics residents' competency level in interpreting emergency radiographs is very important (5).

It has been shown that a clinically significant rate of misinterpretation may occur when radiographs are interpreted with emergency physicians and the rate of misinterpretation is also affected by the level of training and type of radiographs interpreted(6). Emergency medicine faculty and supervised residents are capable of providing highly accurate rates of plain radiograph interpretation when adjusted for clinical significance and actual impact on patient care. Shared responsibility between EM faculty and radiologists operating in an appropriate system serves to prevent adverse patient outcomes as a result of radiograph misinterpretation.

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In addition, the introduction of a quality assurance system also improves image interpretation and avoids adverse patient outcomes from misinterpreted radiographs(7, 8).

Prior studies have revealed differences in physician's capacities in interpreting emergency X-rays compared to reading by radiologists. They have found that formal reporting of ED radiographs by the radiology department detects several clinically important abnormalities that have been overlooked and also detected several incorrect interpretations that may lead to further unnecessary investigations (9-11).

The routine practice of the institution where this study was conducted is that emergency imaging is done at any time in the day. The moment the radiographs are taken, they will be accessible to all through the picture archiving and communication software (PACS) and the referring physician can review the studies even before the patient arrives back to the emergency room. Formal radiologist interpretation may take some time to be available with the study, so those who are handling emergency cases are expected to quickly review emergency imaging for fast decisions. This study then assessed the skill of Paediatric residents in interpreting emergency Paediatric radiographs.

MATERIALS AND METHOD

Methodology

Study design and study population

This study is an institutional-based cross-sectional study done on residents who are being trained in Paediatrics and child health program. All Paediatrics residents at all levels of training were included in the study. There were a total of 83 Paediatrics residents. Among this 32 are year I residents, 32 year II, and 19-year III residents. All residents who consented to participate in the research were included in the study. A total of 79 residents were included.

Data collection procedure

A short survey was done in the Paediatrics emergency section to determine the common emergency visits in the unit that need emergency radiographs. The first 10 common emergency Paediatrics conditions that need radiographs as part of the workup were identified and radiographs were collected from the picture archiving and communication software of the department of radiology which clearly showed the selected 10 conditions. Pictures were changed from DICOM to JPEG format after optimal adjustment of the sharpness and brightness of the images without losing their contrast. Cases then were prepared using PowerPoint slides and questions for each image were printed on paper for participants to write their response.

The responses were corrected based on the interpretations of the same radiographs by a consultant radiologist in the same setting. Then the results were entered into the SPSS version 25.

Data processing and analysis

The collected data were entered into the SPSS version 25 and checked for completeness. Data were analyzed for the correctness of the interpretations and associations were made between accuracy and level of training and confidence of accuracy of interpretations were also assessed.

The overall accuracy of a diagnostic test can be assessed by detecting the Area Under Receiver Operator Curve (AUROC). The Receiver Operator Curve (ROC) is generated by piloting the sensitivity (TP) against 1-specificity (FP). Then the area under the curve was identified. A test that is not better than a chance will lie on a diagonal line with an AUROC of 0.5. The perfect test will have a value of 1. The AUROC of 1 is 100% sensitive and specific. A result less than 0.5 indicates the test is not accurate at all, a value from 0.5 to 0.7 is considered to have low accuracy. A result above 0.7 has medium to high accuracy.

Ethical clearance

Ethical clearance was given from the department research and ethics committee and participation in the study was based on volunteerism and participant identifiers were not used in the data collection and results were displayed in groups.

RESULT

A total of 79 Paediatrics residents were enrolled in this study. The proportion of male residents was 33 (41.8%) with a female proportion of 46 (58.2%). R1 and R2 residents were 32 (40.5%) and 28 (35.4%), respectively, while R3 residents were 19 (24.1 %).63 (79.7%) took radiology training in their undergraduate training but none of them took radiology training during the time of postgraduate trainings.70 (88.6%) of the residents believed that level of training they got is not adequate for interpreting results of the x-ray, and 63 (79.7%) responded they don’t feel capable of reading x-ray results.

Overall score in correctly detecting x-ray findings

The case that was answered correctly by most was the x-ray of intestinal obstruction, by 73 (92.4%) of the residents. Pleural effusion was the second most correctly detected case in 69 (87.3%), followed by lobar pneumonia 67 (84.8%). The case that was missed by most residents was pneumoperitoneum detected by only 11 (13.9 %) of the residents followed by mediastinal mass, which was detected by only 22 (27.8%) of the residents.

Pulmonary edema was also detected only by 23 (29.1%). Another important observation was tension pneumothorax was missed by 30 (38%) of the residents (Table 1).

Table1: The proportion of correct and incorrect interpretation of the cases

Case	Correct n (%)	Incorrect n (%)
Pneumothorax	49 (62)	30 (38)
Normal	34 (43)	45 (57)
Pleural effusion	69 (87.3)	10 (12.7)
Pulmonary edema	23 (29.1)	56 (70.9)
Cavitation and consolidations	39 (49.4)	40 (50.6)
Pneumoperitonium	11 (13.9)	68 (86.1)
Intestinal obstruction	73 (92.4)	6 (7.6)
Mediastinal mass	22 (27.8)	57 (72.2)
Radial fracture	60 (75.9)	19(24.1)
Lobar pneumonia	67 (84.8)	12 (15.2)
Total	**447 (56.6)**	**343 (43.4)**

No resident correctly interpreted all the cases. Two residents correctly identified 9 cases out of the ten. The majority of the residents 47 (59.5%) identified 1-5 of the ten cases. Only 32 (40.5%) identified 6 and above cases correctly (Table 2). As we can see from the table the sensitivity to detect an abnormality on x-ray is 72 (91.1 %). In this case, the specificity is the probability of the resident's in identifying a normal x-ray as normal it is 34 (43%). From the above table we can also drive the following measures: True negative (TN) (n) 43%, false positive (FP), 45 (57%), true positive (TP) (n) 91.1% , and false (FN), 7(8.9%) Table – 2.

Table 2: Number of correctly interpreted cases (overall score out of 10) and the ability of residents' in detecting a normal from abnormal X-rays in general

Categories of correctly interpreted cases		N (%)
Poor skill	1 - 5	47 (59.5)
Good skill	6 - 10	32 (40.5)

Responses of the residents when a normal x-ray is displayed		N (%)
Response	Normal	34 (43)
	Abnormal	45 (57)
Responses of residents when abnormal x-ray is displayed		
Response	Abnormal	72 (91.1)
	Normal	7 (8.9)

The AUROC for the resident's clinical accuracy in identifying a normal from an abnormal x-ray was 0.73. This means the overall accuracy of the residents in identifying a normal from an abnormal x-ray at gross level is 73%, Figure 1.

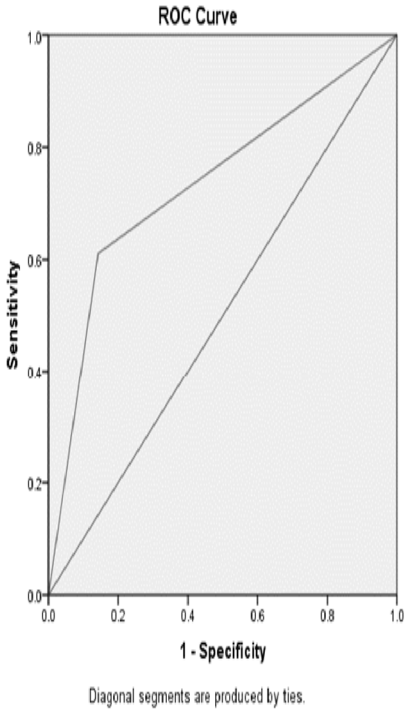

Figure 1: The AUROC for detecting normal x-rays from abnormal.

The sensitivity for clinical skills of the residents in detecting pulmonary edema was 23 (29.1%), and the specificity was 9 (11.4%). The response is remarkable for very high rates of false-positive 70 (88.6%) and false-negative 56 (70.9%) rates. The AUROC was 0.47; indicating the overall accuracy of the residents in detecting cardiogenic pulmonary edema is 47%, even lower than the chance result. The ROC lied almost on the diagonal line.

The sensitivity for detecting lobar pneumonia was 67 (84.8%) and the specificity was 34 (43%). The result is characterized by a high false-positive rate, 46 (57%). The AUROC was 0.49, indicating an overall accuracy of 49%.

The x-ray of pneumothorax was misinterpreted by most residents as pneumonia 9 (30 %), followed by dextrocardia, and CPAM. The normal x-ray was mostly confused with increased pulmonary vascular marking and pulmonary hypertension 19 (42.2 %), Asthma 7 (15.5 %), hilar LAP,7 (15.5 %) and pulmonary edema,6 (13.3 %). The pleural effusion x-ray was missed by only 10 (12.7%) residents, and was read as cardiomegaly in 4(40 %), pneumonia 3(30 %), pneumothorax 1(10 %) and as the right side effusion in 2 (20 %).

The x-ray of pulmonary edema was misinterpreted mostly as Pulmonary TB by 34 (60.7 %) residents and the rest as multifocal pneumonia,14 (25%) which could have significant management difference. The x-ray showing mediastinal mass was also misread mostly as cardiomegaly,16(28.1 %), CHD,15(26.3 %), dextrocardia,7(12.3 %), lung mass,4(7%), PAPVR (scimitar sign) 4(7 %). There were 19 participants who missed radial fracture. The radial fracture was mistaken mostly for ulnar fracture 10(52.6 %), followed by fibular fracture 3(15.8 %), Rickets 2(10.5 %), and chronic osteomyelitis 2(10.5 %). The lobar pneumonia was confused with pleural effusion 9(75 %) and Tuberculosis 3(25 %).

Associations between variables

The rated confidence levels showed only 8.9% of the residents were 100% sure about their interpretation, 44.3% were 75% sure about their interpretation. The level of confidence was below 50% for the rest of 53.2% of the residents. Statistically, a significant association was found with the year of residency and confidence level (P-value = 0.02). 63.2% of R3s' scored above 5, followed by R2s' (39.3%), and R1s' 25%. (P-0.02,OR-3.8). Among those residents whose overall score was <5, 73% had a certainty level of less than 50%. (P-0.044, OR-2.7, CI, 1.02-7.4). However, undergraduate training, duration of clinical service before residency, presence of radiologist while working as GP, and feeling able to read independently did not appear to create statistically significant differences in interpretation skills of the residents (Table 3).

Table 3: Association of skills with variables

		Number of correct responses				
		>5	**<5**			
		n (%)	n (%)	P	OR	95%CI
Year of residency	R1	8 (25)	24 (75)	0.020	3.8	1.2-11.9
	R2	11(39.3)	17 (60.7)			
	R3	12 (63.2)	7 (36.8)			
Level of confidence	<50%	10(27)	27 (73)	0.044	2.7	1.02-7.4
	>50%	21 (50)	21 (50)			
Experience as GP	1-2YRS	26 (40)	39 (60)	0.84	1.14	0.31-4.18
	>2YRS	5 (35.7)	9 (64.3)			

DISCUSSION

This study showed that radiographs with intestinal obstruction, pleural effusion, and pneumonia were the three common diagnoses that were correctly identified by participants. Pneumoperitoneum, mediastinal mass, Pulmonary edema and tension pneumothorax were misinterpreted by most participants. Level of training is positively associated with accuracy of interpretation and undergraduate training, duration of clinical service before residency, presence of radiologist while working as GP and feeling able to read independently did not appear to create statistically significant differences in interpretation skills.

Radiographic examinations frequently contribute important information to the medical decision-making process occurring in the emergency department. Often radiographs are initially interpreted by an emergency medicine physician or Paediatric residents, and decisions are made based on this initial interpretation. In many institutions, the radiographs are subsequently interpreted by a radiologist with some means of resolving discrepancies that arise from this second interpretation(12) or as a quality assurance mechanism.

The reported discordance rate of Paediatrics emergency physicians and radiologists radiograph interpretation have a wide range, varying from 3.7% to 26% with clinically significant discordance rate between 0.8% and 7%. In our study, the overall discordance rate was 34 (43%) which is very high. This may be explained by differences in the sample size, and residents were not given pertinent clinical information which may improve their skill of interpretation by providing clues to the diagnosis. (13-15). The level of training in undergraduate medical education will also contribute to the high discrepancy observed in our study. In almost all Ethiopian Medical Schools, radiology is given as a minor course with only three weeks of attachment.

In our study the sensitivity of the residents in detecting abnormal radiographs was 72 (91.1%) with the specificity of 34 (43%). The false-positive rate was 46 (57%) and the false-negative was 7 (8.9%). The lower specificity coupled with a high false-positive rate decreased the overall accuracy to 73%. Even though the sensitivity of 72 (91.1%) seems to be high, it cannot be used to judge the skills of the residents in interpreting radiographs. This is because telling the radiograph as abnormal at a gross level without further specification can be achieved by even the most junior physicians.

False-positive (overdiagnosis) readings rather than false-negative (underdiagnosis) readings are common among the residents. The higher false-positive rate among the residents strongly correlate with a lack of knowledge and confidence in excluding the presence of abnormal radiographs and setting the patient as not having the suspected abnormality (16).

The significances of sensitivity and specificity are different in different situations and factors, such as the prevalence of the disease. In an area where the prevalence of a disease is very high, specificity is more important than sensitivity. The selected cases in this study also reflect the most common conditions encountered in the emergency department. Similarly, the importance of sensitivity and specificity of clinical skills of physicians is dependent on varieties of factors, such as the need for urgent intervention, the need for aggressive forms of treatment, and others.

Some of the conditions commonly encountered in clinical practice are time-sensitive and need urgent interventions, such as tension pneumothorax. The clinical skills of the physicians should be very sensitive in such situations and specificity may not be as important (17, 18).

In our study, the sensitivity of the residents to detect pneumothorax was 62% with false-positive rate of 38%. Given that pneumothorax is a common encounter, needs urgent intervention, and also easily treatable, physicians should have very high sensitivity to identify it even with physical examination alone before radiographs are requested. Our study showed 38% false positivity. The skill needed to identify pneumothorax from radiographs is not complex. This shows a significant radiographic skill gap in interpreting basic and practical radiographic findings that are very important in emergency decision-making. Therefore, urgent strategies should be implemented to alleviate the problem (15, 19).

In other situations, both sensitivity and specificity are equally important. As an example, a high sensitivity to detect pneumonia is good, but it should as well be specific enough to identify pneumonia from heart failure (19, 20). In our study, the sensitivity and specificity of detecting pneumonia from radiographs were 84.8%and 43% respectively. The false-positive rate was 57% which reduced the overall accuracy resulting in a low total accuracy (AUROC) of 0.49.

The sensitivity and specificity of the residents in detecting radiographic features of pulmonary edema and associated cardiac abnormalities were very low, 23 (29.1%), and 9 (11.4%) with corresponding high false negative and false positive rates, 70 (88.6%) and 56 (70.9%), respectively. AUROC was 0.47. Almost all of the residents who misinterpreted the findings of pulmonary edema misinterpreted it as pneumonia or miliary TB. This shows identifying radiographic features of pneumonia from pulmonary edema is the most difficult commonly encountered problem among the residents (21). One prior study identified certainty on a particular CXR as being associated with the successful interpretation of that CXR which is similar to the finding in our study.(22).

We found out that the skill of radiographic interpretation among Paediatrics residents to be low compared with other studies showing poor sensitivity and a high false-positive rate. This will lead to potential patient mismanagement. The most common confusion among participants was differentiating pulmonary edema and pneumonia and tuberculosis. Participants were not certain about their interpretation of radiographs even if the degree of certainty improved with the level of training. This study is done in single institution and the number of participants is low for extrapolation of the findings. Participants were not given the patients history which contradicts the actual scenario the residents are working which is known to affect interpretations.

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Based on the observations we made in our study, despite the limitations mentioned above, basic interpretation skill training should be in place for all new residents who are joining the program. There should be a mechanism for regular feedback for radiographs interpreted in emergencies which will serve also as a quality assurance mechanism.

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ORIGINAL ARTICLE

NON-AIDS DEFINING AND AIDS DEFINING MALIGNANCIES AND DETERMINANTS AMONG CHILDREN AND ADOLESCENTS LIVING WITH HIV IN ADDIS ABABA, ETHIOPIA

Etsehiwot Shiferaw, MD[1], Tinsae Alemayehu, MD [2,3 *], Daniel Hailu, MD[4] , Gizaw Teka, MD, MPH[5]

ABSTRACT

Introduction: *The highest burden of human immunodeficiency virus (HIV) infection occurs in sub-Saharan Africa. Yet descriptions of oncologic disorders among children living with HIV in the region is limited. The objectives of this study were to describe the prevalence of Acquired immunodeficiency syndrome (AIDS) defining and non-AIDS defining malignancies among children and adolescents living with HIV and under care at a tertiary Hospital in Addis Ababa, Ethiopia.*

Methods: A facility based cross-sectional study was conducted from May 1 – September 30, 2019. There were 323 children and adolescents eligible for the study with their follow-up period spanning from 2000 – 2018. Data was collected using a structured and pre-tested questionnaire and analyzed using SPSS version 25.0 software. Bivariate and multivariate analyses were conducted with 95% confidence interval and P-value < 0.05.

Results: *The prevalence of all types of malignancies in the study population during their follow-up period was 3.4%: AIDS defining (1.55%) and non AIDS defining malignancies (1.85%). Non-Hodgkin's Lymphoma from the AIDS defining and Hodgkin's lymphoma among the non AIDS defining malignancies were the commonest diagnoses. Five of eleven patients achieved cure. Advanced HIV infection correlated significantly with a diagnosis of a malignancy (AOR: 7; 95% CI: 1.5, 34).*

Conclusions: *The prevalence of oncologic disorders in a pediatric cohort living with HIV is described. Advanced infection was associated with the development of malignancies. Early diagnosis and timely initiation of antiretroviral treatment can help prevent the development of cancers in children and adolescents living with HIV.*

Keywords: *HIV, children, adolescents, cancer, Ethiopia*

INTRODUCTION

The Human immunodeficiency virus (HIV) and its Acquired immunodeficiency syndrome (AIDS) were identified in the early 1980s (1). Globally, there were 1.7 million children living with HIV in 2020, of which 53% were on antiretroviral treatment (ART) (2). In Ethiopia, 58,000 children were living with HIV in the same year – only 21,300 of them were receiving ART (3).

Increased survival associated with antiretroviral drugs (ARVs) being more readily available has led to more non-communicable diseases being diagnosed in affected children. HIV-infected children have a higher risk of developing cancers compared to the general population (4). Most of such malignancies are linked with depletion of CD4+ lymphocytes, a loss of immune function and co-infections with oncogenic viruses like Epstein-Barr virus (EBV), Human herpes virus type 8 (HHV-8) and Human Papilloma virus (HPV) (5).

Equally, initiating early ART and immune reconstitution markedly decreases risk of oncologic diagnoses. Data from the Italian registry for HIV Infection confirms that about 449 per 100,000 ART naïve HIV-infected children develop some form of cancer annually while 76 per 100,000 per annum of children on ART do so. Similar benefits from ART were seen among HIV-infected children in the U.S. on therapy for more than two years (6,7).

Kaposi Sarcoma (KS) (1981), non-Hodgkin's lymphoma (NHL) (1985) and Invasive cervical cancer (1992), were the earliest identified AIDS defining illnesses (8) while in subsequent years, various non-AIDS defining cancers have increasingly been identified (9).A multi-center report from pediatric cohorts under HIV care in South Africa showed an incidence of malignancies of 82 per 100,000 person-years during a 29,348 person-years of follow-up period. KS and NHL were the most common malignancies among these cohorts.

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An incidence of 17 per 100,000 was reported for non-AIDS defining malignancies (10). These findings were also backed by Rees et al's review of the epidemiology of KS and NHL among sub-Saharan African children (11). An increased incidence of childhood KS, NHL, nasopharyngeal carcinoma and rhabdomysarcoma also occurred simultaneously with the HIV epidemic in Zambia in the early 1990s (12).

The World Health Organization (WHO) lists the following malignancies as being AIDS defining: KS, Burkitt's Lymphoma (BL), Diffuse Large B Cell Lymphoma (DLBCL), Primary CNS lymphoma (PCNSL), other NHLs - Peripheral T Cell Lymphoma, Primary Effusion/Body Cavity Lymphoma, Polymorphic B cell Lymphoma, Plasmablastic Lymphoma of the Oral Cavity and Cervical cancer (13).

Few data exist on the epidemiology of malignancies in children and adolescents living with HIV in the second most populous African country – Ethiopia. A cohort study on predictors of hospitalization among Ethiopian children on ART showed two of 86 hospitalizations during the study period among 405 patients were to treat KS (14). Existing knowledge on non-AIDS defining malignancies (NADMs) comes from a handful of case reports (15). The objectives of this study were to determine the prevalence and characterization of AIDS-defining and non-AIDS defining malignancies among children and adolescents living with HIV and under care at a tertiary Hospital in Addis Ababa, Ethiopia.

MATERIALS AND METHODS

Study setting and period

The study was conducted from May 1 – September 30, 2019. The study site – the Tikur Anbessa Specialized Hospital in Addis Ababa – is the largest tertiary referral center in Ethiopia. It is a public hospital affiliated with the College of Health Sciences of the Addis Ababa University. Its pediatric infectious diseases' clinic provides care for 512 children and adolescents living with HIV. Its pediatric hematology/oncology unit is the main referral center for treatment of children with malignancies from all over Ethiopia. Until recently, it served as the only pediatric cancer treatment center in the country.

Study design

An institution based retrospective cross-sectional study was implemented using chart reviews to determine the prevalence of AIDS defining malignancies (ADMs) and non-ADMs in the study population.

Sample size

All children and adolescents (0 – 18 years) under HIV care in the clinic were considered for enrollment into the study. Since there are no baseline epidemiologic studies conducted in this topic in Ethiopia, we used the following formula to calculate a sample size of 384 - taking the reference p value as 0.5 (50%) and a margin of error of 5%.

$n = z^2 \times p \times (1 - p)/d^2$; $z = 1.96$, $p = 0.5$, $d = 0.05$

We then gave a 15% estimate for incomplete records, leaving a final sample size of 326 children and adolescents.

Data collection and quality control

A structured and pre-tested data collection tool was prepared using selected demographic and clinical variables extracted from chart reviews. Data collection tool was tested on 5% of the estimated sample size (n = 16). Trainings were given for data collectors (medical interns who have received comprehensive HIV care and treatment trainings during their clinical courses) on data collection. The sample population (n = 326) were recruited by enrolling the first two children and leaving out the record of the third child and repeating the sequence for the entire set.

The principal investigator checked the data for completeness once a week. Further quality checks were performed by structured checklist set as a reminder for data collectors at the completion of each data set; as well as during data analysis.

Statistical analysis

Data was cleared, coded and exported to the SPSS statistical software version 25 for analysis. Descriptive statistics were used to outline magnitude of the problem while bivariate and multivariate analysis were utilized to identify predictors of the primary outcome. A 95% CI and a p-value of less than 0.05 were set as threshold for statistical significance.

Ethical considerations

The study protocol was approved by the Research and Publications Committee of the Department of Pediatrics and child health, College of Health Sciences, Addis Ababa University. Anonymity was ensured as retrieved and analyzed data was devoid of names, telephone numbers and chart number of patients.

RESULTS

Demographic and clinical description of the study population

Three hundred twenty three participants were eligible for the study. The mean age of participants was 13.6 years (SD 3.4).

Males accounted for 52.9% (171) of the study population.

A diagnosis of HIV infection was made before five years of age for 61% (167) of children. All were receiving antiretroviral drugs (ARVs) (table 1).

Table 1: Socio-demographic characteristics of study participants

Variables	Category	Frequency (n = 323)	Percent
Sex	Female	152	47.1
	Male	171	52.9
Residence	Addis Ababa	286	88.5
	Outside Addis Ababa (Urban)	10	3.1
	Outside Addis Ababa (Urban)	27	8.4
Age category	Less than 5 years	11	3.4
	5 - 10 years	42	13.0
	11 - 14 years	109	33.7
	15 - 18 years	162	49.8
Age at diagnosis of HIV infection	Less than 5 years	197	61.0
	5 - 10 years	106	32.8
	11 - 14 years	20	6.2

Two-thirds of our cohort (69.7%) had CD4 counts of more than 350/mm^3 in their latest determinations while 140 (43.3%) had stage three and four WHO clinical stages.

The majority were on NNRTI-based ART during the study period. Fifty (15.5%) children and adolescents had had a failed first line ART regimen, of which half had virologic failure (table 2).

Table 2: Clinical characteristics of study participants

Variables	**Category**	**Frequency (n = 323)**	**Percent**
CD4 at initiation of ART (/ mm3)	Less than 200/mm3	53	16.4
	200 – 350/mm3	45	13.9
	350/mm3 and above	225	69.7
WHO clinical stage during study period	Stage I	69	21.4
	Stage II	114	35.3
	Stage III	78	24.1
	Stage IV	62	19.2
ART regimen study participants were taking during study period	NNRTI-based	284	87.9
	PI-based	39	12.1
Duration on ART	Less than 5 years	88	27.2
	5 years or more	235	72.8
Failed first line ART regimen	Yes	50	15.5
	No	273	84.5
Type of failure in those who have had a failed first line ART regimen (n = 50)	Virologic	25	
	Immunologic	5	
	Clinical	1	
	Combined	19	

Key: NNRTI - Non-nucleoside reverse transcriptase inhibitor; PI – Protease inhibitor

Epidemiology and determinants of malignancies in the study population

The prevalence of all types of malignancies was 3.4% - with a 1.85% prevalence for NADMs and a 1.53% prevalence for ADMs. The commonest clinical presentation in children and adolescents with an oncologic diagnosis was a body swelling. There were ADM diagnoses in five children, all being NHLs. Among NADMs, HL was the commonest (4/6). The time lapse following initiation of ART till diagnosis of an oncologic malignancy (ADM or NADM) was less than one year in 4/11 children. Five of eleven patients achieved cure for their malignancies while a further five died due to their cancers or chemotherapy related complications (table 3).

Table 3: Clinical characteristics of study participants with diagnosed cancers

Variables	Categories	Frequency (n = 11)
Presenting clinical feature for diagnosed cancers	Body swelling	9
	Bleeding tendencies	1
	Cough and difficulty of breathing	1
Type of cancers	ALL	1
	HL	4
	NHL	5
	RMS	1
Time lapse following initiation of ART till an oncologic diagnosis	Simultaneous diagnoses	3
	Less than 1 year	4
	1 – 5 years	2
	5 years and more	2
Outcome of treatment for cancers	Cure	5
	Ongoing treatment	1
	Death	5

Key: ALL - Acute lymphoblastic leukemia, HL – Hodgkin's Lymphoma, NHL – Non-Hodgkin's Lymphoma, RMS – Rhabdomyosarcoma

Following bivariate and multivariate analysis, advanced HIV infection (WHO clinical stages 3 and 4) were noted to correlate with a diagnosis of a cancer. Children and adolescents living with advanced HIV infection (stages 3 and 4) were seven times more likely to have an oncologic diagnosis than those with WHO clinical stages 1 and 2 (table 4).

Table 4: Multi-variate analysis of factors associated with oncologic diagnoses

Variables	Categories	Presence of cancer		COR (95% CI)	AOR (95% CI)	p-value
		Yes	No			
Sex	Female	2	150			
	Male	9	162	4.2 (1.5, 11.5)	4.4 (0.9, 21)	0.066
Duration on ART	Less than five years	4	145	0.64 (0.28,1.45)	0.5 (0.15, 2)	0.40
	Five years and more	7	216			
WHO clinical stage	Stages 1 & 2	2	181			
	Stages 3 & 4	9	131	6 (2.3, 17)	7 (1.5, 34)	0.015
Failed 1st line ART regimen	Yes	2	48	1.2 (0.4, 3.4)	1.1 (0.2, 5.2)	0.97
	No	9	264			

Key: AOR – Adjusted odds ratio, COR – Crude odds ratio, CI – Confidence interval

DISCUSSION

Our study showed that 3.4% of the children and adolescents receiving HIV treatment and care in the study hospital had or have a diagnosis of ADM or NADM during their follow-up period. This fares poorly in comparison to the 71 children (0.6%) which had a diagnosis of cancer among a cohort of 11,707 children in two South African pediatric HIV clinics (10). It is also twice that was reported by Mbulaiteye et al (7/407) from the Uganda AIDS-Cancer registry (16). The high prevalence may be due to the reason that Tikur Anbessa specialized hospital is the main treatment center for children with malignancies from all over Ethiopia and it remained the only unit to do so in the country till recently.

Among our study population, the most common identified NADM was HL while all of the ADMs were NHLs. No cases of KS were diagnosed. This was in contrast to a multi-center case-control study conducted in four sub-Saharan countries (Botswana, Malawi, Tanzania and Uganda) where 83.8% of the 451 malignancies among children living with HIV over a 13 year period were KS (17). NHLs were the second most common oncologic diagnosis in the aforementioned east and southern African reports. Differences in KS epidemiology can be attributed to the fact that ours was a single-center study with a smaller study population.

We also observed that the odds for having a diagnosis of a cancer were higher in advanced HIV infection (WHO stages 3 and 4). People with untreated and progressing HIV infection have chronic antigenic stimulation, inflammation and cytokine dysregulation leading to development of lymphomas and other ADMs (18).

Bohlius et al noted (among their cohorts in pediatric HIV clinics in Johannesburg and Cape Town, South Africa) that those initiated on ART before two years of age had a four to five times higher risk for developing cancers versus children aged 2 years and above at ART initiation. No such correlations were seen in our study (10).

Close to half of children who developed various cancers achieved cure after initiating treatment. Cancer mortality is high among children living with HIV in Africa. Median survival in children and adolescents living with HIV and diagnosed with KS was less than six months in a recent trial from Malawi (19). In Uganda, median survival in HIV-infected children with Burkitt lymphoma was less than a year (11.8 months) (20).

High mortality rates in sub-Saharan countries may be related to delayed presentations, inadequate diagnostic and therapeutic modalities. Davidson et al from the South African Children's Cancer Study Group analyzed 288 children living with HIV with malignancies and determined that more than 80% presented with advanced disease. Their overall survival was 33.7% while it was 57.8% for those who received ART and chemotherapy (21). The aforementioned diagnostic gap which also prevents monitoring of drug toxicities as well as deficiencies in the armamentarium of chemotherapeutic and antiretroviral drugs which may help overcome harmful drug-drug interactions also shortens patient survival (22).

Conclusions

This is the first study looking into the epidemiology of malignancies in children and adolescents living with HIV in Ethiopia. It shows a high prevalence of oncologic diagnoses in a pediatric cohort living with HIV at the country's largest tertiary referral hospital. Advanced infection predicted development of a malignancy in the study population. Our study is limited by a small sample size which reflects the small overall numbers of children living with HIV nationwide (total of 58,000 in the country; 1% of which are under follow-up at the study hospital). Further multi-center studies are required as more and more joint pediatric HIV and oncology clinics start their service in other referral hospitals in Ethiopia. Efforts to improve early diagnosis and timely initiation of anti-retroviral treatment help prevent the development of cancers in children and adolescents living with HIV.

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Conflict of interests

The authors declare they have no conflict interests.

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ORIGINAL ARTICLE

ASSESSING THE PROGRESS OF PRIMARY MEASURES TO PREVENT COVID-19 TRANSMISSION AT THE GATES OF A TERTIARY HOSPITAL IN ADDIS ABABA

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ABSTRACT

Introduction: *COVID-19 is a major global threat. A proven way to decrease its spread is by applying preventative measures such as proper physical distancing, hand hygiene and respiratory hygiene practices.*

Objective: *To assess the status of measures to prevent COVID-19 transmission by patients, attendants and health care workers at the gates of Tikur Anbessa Specialized Hospital.*

Methods*: An institutional based cross-sectional study was conducted on all patients, attendants, health care workers and support staff entering the premises of Tikur Anbessa Specialized Hospital between 7:45 to 9:30 am via three gates from June 22 to August 30, 2020. A systematic random sampling method was employed to select 20 participants from each gate to observe twice weekly the status of individual behavior on hand and respiratory hygiene and physical distancing.*

Results*: Overall, 1000 individuals were involved in the study. From this 568 (56.8%) were men. The majority 79.6 (79.6%) were in the estimated age group (by observation only and not asked) of 18 to 50. Altogether, the practices of proper hand hygiene, proper physical distancing and proper utilization face mask were 10.7%, 77.3% and 86.9%, respectively, over the period of 10 weeks.*

Conclusion*: There was an overall good practice of social distancing and mask usage. On the contrary, hand hygiene practice was remarkably low. Enforcement issues and shortage of infrastructures were key challenges observed in this study*

Key words*: Covid-19, Tikur Anbessa Specialized Hospital, physical distancing, respiratory hygiene, hand hygiene*

INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a new strain that has not been previously identified in humans and is the cause of COVID -19.(1) Common transmission routes include direct transmission (cough, sneeze, and droplet inhalation transmission) and contact transmission (contact with oral, nasal, and eye mucous membranes). (2) This emerging respiratory disease was abbreviated as COVID 19, after it has been first reported in December 2019 in Wuhan city of China. (3) As of September 28, the pandemic has infected more than 33 million people with upwards of 1,002,394 deaths. (4)

In Ethiopia the first corona case was confirmed on March 1, 2020 March and as of September 28, 2020 there are 73,944 infected cases and 1,177 death.(4) In response to this pandemic, the government declared a state of emergency on April 8. Subsequently, several essential measures were taken including mandatory quarantine periods for travelers, restrictions on public gatherings, school closures, mandatory facemasks, physical distancing in public places, hand hygiene practice at entrances of public, fewer passengers using public transport and risk communication on prevention. Similarly, Tikur Anbessa Specialized Hospital (TASH) has made strides by forming an Emergency Operating Committee (EOC) on March 16 with the main objective of prevention, control and management of the disease in the hospital. To effect this smoothly in the midst of the pandemic it is collaborating with key stakeholders like the Ministry of Health to design locally contextualized effective prevention and intervention.

(6)Some of its work are installing hand hygiene facilities at different areas, thermal temperature screening, limiting the number of attendants, labeling the gates based on use, mandating universal masking, ensuring physical distancing and hand hygiene at entrances. Despite all these efforts, there has been a progressively increasing number of confirmed cases among patients, attendants and staff of the hospital.(7)

When faced with similar predicaments in other hospitals of the country, a multicenter study was done and showed poor practice of the preventive measures relative to other countries despite good knowledge and positive attitude.

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The shortage of infrastructure had been implicated as possible reasons for this difference. (8)However, there is only limited data regarding this subject, especially in our country's set up including TASH.

This study aims to determine the magnitude of proper mask utilization, hand hygiene and physical distance practices at the gates of TASH. It will also identify challenges for implementation of these practices as it could potentially be used as ancillary data for future studies.

MATERIALS AND METHODS

Study area: The study was undertaken at the 3, out of 4 gates of TASH ; i.e. Gate 1 (Fana gate), Gate 2 (Staff gate) and Gate 3 (Merkato Gate). Since the era of COVID-19, regulations at TASH have been more stringent regarding its four entrance gates. Gate 1 is strictly designated for the entrance of patients and attendants. Gate 3, is also designated for this same purpose. Whereas Gate 2 and Gate 4 also called Staff gates are solely for the entrance of health care workers and support staff members. Gate 4 was not included in the study as it has only been opened in recent times and is rendering its services currently at a low flow of staff compared to Gate 3.The study was done from June 22 to August 30, 2020, stretched over 10 weeks.

Study design*:* An institution based repeated cross-sectional weekly survey was conducted. There were twice observation involving week day and weekend. Monday was chosen for its regular maximum flow of patients through the gates. Saturday was taken to consider the variability with the week day. Hospital records and pilot survey were used to decide on the observation days.

Study subjects: The source population for this study was all patients, attendants, health care workers and support staff entering TASH premises via gates 1, 2, and 3 on Monday's and Saturday's All patients, attendants, health care workers and support staff entering TASH premises via gates on Monday's and Saturday's were observed.

Sampling procedure: A systematic random sampling method was used to select 20 participants from each gate.

Data collecting instruments*:* anonymous observers were standing inconspicuously around the gates to observe individuals behavior on primary preventive practices. This observation technique was chosen to establish uncontrolled behaviors during the entrance to the hospital.

A brief checklist containing sex, estimated age group (by observation only and not asked) , practice of preventive measures (hand hygiene, physical distancing, and respiratory hygiene) was used to collect data. The checklist and the observation technique were pre-tested to ensure their validity.

Operational definitions: the following WHO definitions were used for this study (9, 10).

- **Proper physical distance** means at least 1m distance between the individuals.
- **Proper hand hygiene** means washing one's hands with soap and water for 20 seconds or using alcohol-based hand sanitizers.
- **Proper respiratory hygiene** means wearing a face mask that covers the entire nose, mouth and chin.

Data management and analysis*:* the data was filled, stored and analyzed with MS- excel. Descriptive statistic was used to analyze the data.

Ethical consideration: Confidentiality and privacy were carefully kept up all through the whole study time frame.since this was a covert research with no direct involvement with patients and human kind . As such a proper ethical clearance from the college IRB was found not necessary.

RESULTS

Sociodemographic data

A total of 1000 individuals were observed in this study. From this 568 (56.8%) were men and the remaining 432(43.2%) were female. The majority 79.6% were in the estimated age group (by observation only and not asked) of 18 to 50 while those below 18 and those above 50 comprised 3.2% and 17.2% respectively.

The status of physical distancing, respiratory and Hand hygiene practice

Overall, only 10.7 % of them had proper hand hygiene. Comparing among the gates, gate 3 had the highest performance with average practice of 11.4% while gate 2 and gate 1 had respectively rate of 10.3% and 7.3%.

The trend of hand washing practice during the first 4 weeks was very low and declining, it started to pick up at the end of the 4th week, reached about 50% on week 6, then declined rapidly and leveled off at week 9.

Table 1: Sociodemographic data of individuals observed at the entrance gates, TASH, 2020

Site	Sex		Estimated Age Group		
	Male# (%)	Female# (%)	<18 # (%)	18-50 # (%)	>50 # (%)
Gate 1	242(24.2)	158(15.8)	11(1.1)	313(31.3)	76(7.6)
Gate 2	94(9.4)	106(20.6)	0	175(17.5)	25(2.5)
Gate 3	232(23.2)	168(16.8)	21(2.1)	308(30.8)	71(7.1)
Total	568(56.8)	432(43.2)	32(3.2)	796(79.6)	172(17.2)

Gate 1 & 2: Patient entrance; Gate 3: staff entrance

Regarding physical distancing, the average practice percentage of all the gates was 77.3 percent. Individually, there was performance of 69.8%, 81.1% and 79.9% at gate 1, 2 and 3 respectively. There was comparable result among weeks with highest record of 84% on week 3 and lowest on week 8.

Among all observed 86.9% had proper face masking. Gate one and two had result of 90.3% and while gate three had the least practice (80.5%).

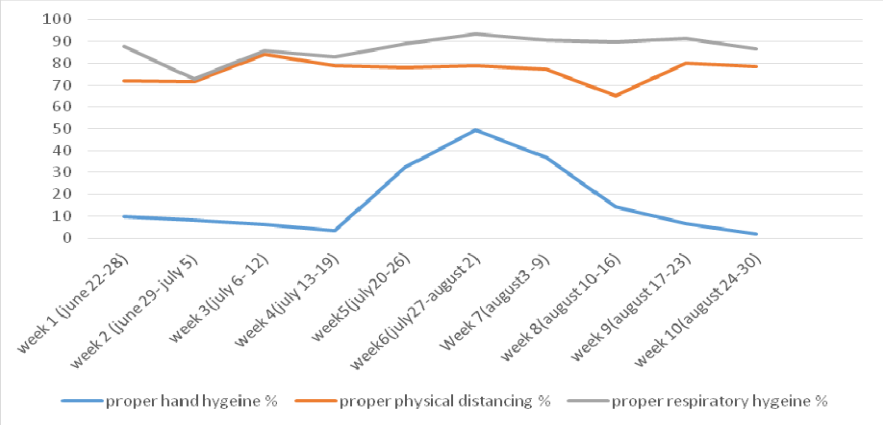

Figure 1: Weekly variations of covid-19 preventive measure practices at the entrance gates of TASH, 2020

Additional observational data

There was inadequacy and misuse of hand hygiene facility at all gates with some improvement observed on week 5 and 6. Service rendering areas like washing basins, thermal screening, information desk, and areas just outside the gates were particularly overcrowded. In addition, some people were entering without their temperatures checked. There were no adequate posters and reminders. For the most part, there was a lack of enforcement at all the gates

DISCUSSION

As per the recommendation of WHO, implementation of preventative measures such as proper physical distancing, hand hygiene and respiratory hygiene is imperative to slow down the pandemic. As such, application of these measures was studied at the gates of TASH.

The practice rate of hand hygiene was found to be only 10.7% which was much lower as compared to studies done in Addis Zemen Hospital (65.5%) and Jimma (77.3%) (11, 12). This could be highly attributed to the shortage in facilities and inconsistent enforcement and in part due to the additional observations listed on the result as well as the difference in the study methodology.

There was a great upsurge in the hand hygiene practice in week 5 and 6.i.e from 3.3 to 49.2. This was the time where good provision of water and soap were observed and the people assigned at the gate like security guards, staffs assigned for thermal screening were making sure each person had washed their hands, wore masks and had proper social distancing. But as soon as the enforcement got loose, the practice regressed dramatically in the weeks to follow from week 7 to 10. This underlines the need for constant monitoring and adequate provision of necessary facilities.

The hand hygiene practice at the staff gate was 10.3% which was much lower than the hand hygiene practice of health care workers elsewhere in Ethiopia (81.4%). (8) Owing to this is the fact that security guards and thermal screening workers felt uncomfortable enforcing the measures to the staff that are mostly health care workers and are thought to have good knowledge about the issue. Meanwhile, gate three had better performance as the enforcement was implemented to a better extent**.**

There was an overall proper social distancing rate of 77.3% at all the gates. This result was much higher than other studies done in Ethiopia where the practice ranges from 22 to 33.6%.(8, 11, 12)This could be greatly attributed to the restriction in the number of attendants per patient, labeling of gates based on their use, use of phone clinics and longer appointment to decrease non-critical hospital visits. Due to these measures number of people entering the gates decreased from 20000 to 7000.

However, there was crowding of people around areas of service provision such as, the information desk, thermal screening section and hand washing basins. Looking at the graphs, there was no significant variation throughout the study as that of the other studies, supporting the above possible explanation. Regardless, the lack of enforcement and even worse looking crowding just outside the gate should not be ignored.

Similarly, better face masking was found (86.9%) than a study done in Addis Zemen Hospital (36.6%) while it was lower than a study done in China where nearly all the participants (98.0%) wore masks.(11) This could be due to the mandating of universal masking by the government. However, it was not satisfactory as some people entered with no mask or using scarves as one.

The strength of this study is it is the first study which assessed the progressive practice of preventive methods of COVID using weekly cross-sectional survey. There were some limitations. The study did not assess associated factors for the practice and discussion of the results were difficult as there are only few studies done in Ethiopia.

Conclusion and Recommendation

There was an overall good practice of social distancing and mask usage. On the contrary, hand hygiene practice was remarkably low. Enforcement issues and shortage of infrastructures were key areas to be improved.

We recommend giving attention to and improving the hand hygiene practices by increasing provision of water and soap facilities close to the Gates. Moreover, placement of printed posters that help raise awareness about handwashing at the columns of the Gates can be supplementary. Giving comprehensive and organized training for the security guards and support staffs working on the gate is another essential step. Lastly, regular supervision and feedback regarding the enforcement of preventive measures is to be highly emphasized on to ensure the sustainability of the efforts made.

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Naghmeh Mostafaee, ElnazSheikhpour, Mahmoud Akhavan, Fatemeh Daneshmand, Azam Hashemi. *Ethiop Med J, 2021, Vol. 59, No. 3*

ORIGINAL ARTICLE

IMMUNOHISTOCHEMICAL EXPRESSION OF BCL-2 AND EPIDERMAL GROWTH FACTOR RECEPTOR (EGFR) BIOMARKERS IN UROTHELIAL CARCINOMA OF THE BLADDER LESIONS

Naghmeh Mostafaee, Msc[1], ElnazSheikhpour, PhD[2], Mahmoud Akhavan, [3], Fatemeh Daneshmand [1], Azam Hashemi*[2]

ABSTRACT

Introduction: *Over-expression of Bcl-2 and* ***Epidermal growth factor receptor (*** *EGFR) is seen in many malignancies. However, evidences regarding the expression of these biomarkers in bladder tumors are limited. The aim of this study was to evaluate expression of Bcl-2 and EGFR biomarkers in benign and malignant tumors of urothelial carcinoma of bladder.*

Methods: *This case control study was conducted on 57 bladder tumors (40 malignant tumors and 17 benign tumors) in Shahid Rahnemoun hospital, Yazd, Iran during 2016-2018. Immunohistochemistry method was used for assessing EGFR and bcl-2 expression in tissue tumors.*

Results: *Among all the study participants, the expressions of EGFR and bcl-2 were found to be positive in 10 (17.4%) and 25 (44%) of cases respectively. There was no significant difference between benign and malignant tumors in terms of EGFR (p=0.830) and bcl-2 expression (p=0.094). The mean EGFR in low and high grade was 4.13± 13.22 and 7.69± 26.26, respectively (p= 0.91). The mean bcl-2 in low and high grade was 3.72± 12.81 and 13.31±26.14, respectively (p=0.51). Significant difference was seen between two groups (benign and malignant groups) regarding age and tumor size (p<0.05).*

Conclusion: *According to results of current study, no significant difference was seen between benign and malignant tumors in terms of EGFR and bcl-2 expression. Thus, assessment of these two biomarkers is not proposed in bladder tumors. Moreover, no relation was seen between EGFR and Bcl2 expression with grade. Therefore, expression of these biomarkers didn't affect on grade of the tumor.*

Keywords: *Bcl-2, Biomarkers, Bladder carcinoma, Epidermal growth factor receptor*

INTRODUCTION

Bladder cancer is considered as the fifth most common cancer in the world and the second most common cancer in some areas of Iran (1). The worldwide incidence of bladder cancer is 350-400.000 new cases per year (2). It is assessed that more than 560,000 bladder cancer patients live in United States (3). The incidence of bladder cancer in men is higher than women (4). Common risk factors include cigarette smoking (5-8), certain chemotherapeutic agents, and aromatic hydrocarbons.

Urothelial carcinoma (transitional cell carcinoma) is the most common type of bladder cancer (9). Adenocarcinoma and squamous carcinoma are other types of bladder cancer (4). Sensitive and accurate detection of bladder cancer is critical to diagnose the disease at early stage.

In addition, prediction of prognosis, recurrence, and response to therapy is necessary. Although urine cytology remains as the gold standard technique, several new urinary biomarkers that may help in the diagnosis, prediction of treatment response, and prognostication of the disease have been identified (10).

Abnormal expression of epidermal growth factor receptor (EGFR) is seen in many human cancers. It is considered as a poor prognostic marker (11). This receptor is the product of c-erbB1 proto-oncogene and belongs to type 1 tyrosine kinase receptor family (12). Studies reported assessment of EGFR expression in limited population. Furthermore, bcl-2 protein as a proto-oncogen plays a main role in inhibition of apoptosis.

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Expression of Bcl-2 is seen in many tumors including breast (13), prostate, and head and neck tumors (13). It contributes in oncogenesis by repressing signals that induces apoptotic cell death (14). Its expression is associated with poor prognosis, resistance to current treatment modalities including radiotherapy and hormone therapy in advanced prostate cancer (13).

Enache et al., demonstrated immunoexpression of EGFR in 53.3% of cases of bladder cancer (15), but Hashemi et al., showed lack of EGFR expression in 58.7 % of cases (11). Krish et al. reported that Bcl-2 overexpression is rare in bladder transitional cell carcinoma (16). Korkolopoulou et al. evaluated expression of bcl-2 proteins in bladder carcinomas and showed that 44% of patients were bcl-2 positive (17).
Studies conducted regarding the expression of Bcl-2 and EGFR biomarkers in urothelial carcinoma of the bladder lesions were few and controversial (16-19). So far, no study was conducted regarding expression of these biomarkers in malignant and benign tumor in this area and it was not specified if we can use the expression of these biomarkers for detection of benign and malignant tumors. The aim of this study was to evaluate the immunohistochemical expression of Bcl-2 and EGFR biomarkers in urothelial carcinoma of the bladder lesions and its relation to grade.

MATERIALS AND METHODS

Sample selection and histopathological analysis
This case control study was conducted on bladder tumors in Shahid Rahnemoun Hospital, Yazd, Iran. Paraffin blocks of bladder tumors of benign and malignant groups were taken from Department of pathology. The sample size was assessed according to Cochran formula.
Data of patients (17 benign tumor and 40 malignant bladder tumors) were extracted from medical records. Then paraffin embedded samples were taken from pathology department of Shahid Rahnemoon Hospital, The histopathological diagnosis was performed by criterions according to Lopez et al., 2004 (19). Tumor grade is classified into three groups (grade I, grade II, grade III).

Immunohistochemical analysis of EGFR and Bcl2
Immunohistochemistry method was used for diagnosis of EGFR and Bcl2 biomarkers in tumor samples by poly-L-lysin coated slides. After mounting 3 µm thick histological sections on slide, they were dewaxed at temperature of 60^0C and rehydrated with decreasing concentration of alcohol. Hydrogen peroxide (0.3%) was used for blocking the endogenous peroxidase activity in tissue samples. After washing with tris Then, the sections were exposed with primary antibody (Bcl2 and EGFR antibody) which is prepared from Abcam Company (according to the protocol). In the next step, slides were incubated with secondary antibody (rabbit-mouse antibody) according to DAKO protocol (Denmark). These sections were then incubated with 3, 3-diamino-benzidine tetrahydrochloride and substrate for 10 min and placed in hematoxylin solution for 1 minute and rinsed in tap water. Finally, these slides were immersed in graded alcohol, xylene, and mount.

Statistical analysis
Data were entered into SPSS version 22. Mann Whitney U Test and Chi Square test were used for analysis of data. $P<0.05$ was assumed significant.

Ethical consideration
After obtaining consent from patients, current study was approved by Ethical committee of Shahid Sadoughi University of Medical Sciences.

RESULTS

In current study, 57 patients with bladder tumors were chosen in Shahid Rahnemoun hospital. Frequency of parameters including tumor type, grade and sex is shown in Table 1.

Table 1: Frequency of parameters with bladder cancer

Parameter	Classification	Frequency	Percent
Tumor	Malignant	40	70.2
	Benign	17	29.8
Grade	Low	22	55
	High	18	45
Sex	Women	12	21.1
	Men	45	78.9

As shown in Table 1, 70.2% of tumors were malignant. Moreover, frequency of patients in terms of gender showed that 80% of malignant tumors belonged to men and 20 % of them to women.

The parameters including tumor size, age, tumor size, EGFR, Bcl2 in patients with bladder cancer is shown in Table 2.

Table 2: The parameters in patients with bladder cancer

Parameters	Mean± SD	Min	Max	p-value
Age				
Malignant Benign	64.8±2.33	33	90	0.032
	55.53±3.5	28	79	
Tumor Size				
Malignant	1.85± 0.27	0.3	10	0.025
Benign	1. 51± 0.59	0.3	10	
EGFR				
Malignant	6.5± 3.23	0	95	0.840
Benign	8.23± 5.89	0	90	
Bcl2				
Malignant	7.07±2.8	0	80	0.119
Benign	22.06± 7.36	0	10	

Frequency distribution of patients in terms of EGFR showed that among 40 malignant tumors, eight (20%) were EGFR positive. In addition, among 17 benign tumors, two (11.7%) were EGFR positive. Totally, among 57 tumors, 10 tumors (17.4%) were EGFR positive.

Moreover, frequency distribution of EGFR showed that there was no significant difference between benign and malignant tumors in terms of EGFR expression (Chi-Square test) (P=0.830).

In addition, frequency distribution of patients in terms of bcl-2 showed that among 40 malignant tumors, 16 tumors (40%) were bcl-2 positive. In addition, among 17 benign tumors, 9 (52.9%) were bcl-2 positive. Totally, among 57 tumors, 25 tumors were bcl-2 positive (44%). No significant difference was seen between two groups (benign and malignant groups) regarding Bcl-2 (P=0.094).

Table 3: The expression of EGFR and Bcl2 in terms of grade

Bio-marker	Low grade Mean ± SD	High grade Mean ± SD	P-value
EGFR	4.13± 13.22	`7.69± 26.26	0.91
Bcl2	3.72± 12.81	13.31±26.14	0.511

The minimum and maximum of EGFR in low grade and high grade was 0-60 and 0-95, respectively. In addition, the minimum and maximum of Bcl2 in low grade and high grade was 0-60 and 0-80, respectively As shown in Table 3, no significant difference was seen between EGFR and Bcl2 expression in terms of grade (P>0.05).

DISCUSSION

The prevalence of bladder cancer is high in Iran (1) and studies regarding the role of EGFR and bcl2 expression in bladder cancer were controversial (14-19).

Moreover, the expression of EGFR and bcl2 in bladder cancer has not been studied in the region. Therefore, we evaluated expression of these biomarkers in benign and malignant tumors of bladder and observed that among 40 malignant tumors, eight tumors (20%) were EGFR positive. In addition, among 17 benign tumor, two (11.7%) were EGFR positive. Totally, among 57 tumors, 10 tumors (17.4%) were EGFR positive. Hashemi et al., evaluated the expression of EGFR in urinary bladder cancer and observed high expression of EGFR in 26.2% of cases (11). Hashemi et al. reported that EGFR was over-expressed in 26.2 % of bladder cancer tissue specimens (20). Enache et al., demonstrated immunoexpression of EGFR in 53.3% of cases of bladder cancer (15). The findings of various studies indicate different results.

In addition, there was no relation between EGFR expression and grade. Hashemi et al, assessed the prognostic value of EGFR in urinary bladder cancer and observed a significant relation between EGFR expression and grade of disease (11) which was inconsistent with our study. It seems that one reason of difference between two studies was due to sample size. Our study consisted of 40 bladder cancer patients, while Hashemi et al., considered 126 cases of bladder cancer. Railkar et al. showed a high amplification rate of EGFR in most bladder cancers. Therefore, they proposed treatment of EGFR expression in bladder cancer with EGFR Targeted Photoimmunotherapy (PIT). It is believed that this method may offer a selective and new therapy for non-muscle invasive bladder cancer (21). Rebouissou et al. reported that basal phenotype which is enriched with EGFR was found approximately in 25% of bladder tumors (22). It seems that tumors with EGFR expression can be candidate for cancer treatment.

Moreover in our study, expression of bcl-2 was observed in 44 % of patients with bladder cancer. In current study, there was no significant difference between two groups, considering bcl-2 expression. Korkolopoulou et al. evaluated expression of bcl-2 proteins in bladder carcinomas and observed that 44% of patients were bcl-2 positive (17) which is consistent with our findings. Krish et al. also demonstrated that Bcl-2 overexpression is rare in bladder carcinoma (16).

The finding of this study is inconsistent with our study. It seems that factors including gender, race, type of tumor, and geographical region are influential factors on different expression of bcl-2(16). Swellam et al. evaluated the incidence of bcl-2 expression in malignant bladder tumors (57 tumors with squamous cell carcinoma and 61 tumors with transitional cell carcinoma) and showed a potential role of bcl-2 expression in carcinogenesis. Moreover, they proposed that anti-bcl-2 therapy may be useful for these patients (14). Cho et al. reported that over-expression of bcl-2 protein in bladder cancer inhibited cisplatin-induced bax translocation (23).

In addition, we did not find any relation between grade and bcl-2 expression. Swellam et al., observed no relation between bcl-2 expression and histological grade which was consistent with our study (14). Korkolopoulou et al. reported that bcl-2 expression was not related to grade, in consistence with our study (17). Cook et al. achieved similar findings and reported no significant relation between tumor grade and bcl-2 expression (13). Therefore, most studies reported no relation between bcl-2 expression and grade; while Ricardo Gonzalez-Campora et al. found that bcl-2 over-expression was associated with low grade malignancy (24). Therefore, studies in this regard were controversial and need more research.

In addition, tumor size in patients with malignant bladder carcinoma was significantly greater than benign bladder carcinoma. Thompson et al. reported that the risk of malignancy tumors increases with tumor size (25). The finding of this study is consistent with our study. Cheng et al. reported that tumor size had important role for predicting metastasis free survival (26). The comparison of two groups in terms of age showed that the mean age of patients in malignant group was significantly higher than benign group. White et al. reported that cancer is an age-related disease because the occurrence of cancers increases with age. The finding was consistent with our study (27). The incidence of cancer in older ages poses unique challenges to attaining a high quality of life. Brandt et al. reported that age is a main risk factor for breast cancer (28).

Conclusion

According to results of current study, no significant difference was seen between benign and malignant tumors in terms of EGFR and bcl-2 expression. Thus, assessment of these two biomarkers is not proposed in bladder tumors. Moreover, no relation was seen between EGFR and Bcl2 expression with grade. Therefore, expression of these biomarkers didn't affect on grade of the tumor.

Conflict of interest

There is no conflict of interest

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ORIGINAL ARTICLE

PREVALENCE AND RISK FACTORS OF NEONATAL STUNTING AMONG NEONATES AT TIKUR ANBESSA SPECIALIZED HOSPITAL

Handsome Deksiso MD[1], Amha Mekasha MD, Msc [1*]

ABSTRACT

Introduction*: Stunting is widely used to assess nutritional status of children but not in neonates. Neonates with fetal growth restriction are at risk of being stunted at 24 months and development of non-communicable diseases during adulthood. Under-nutrition during the first 1000 days post conception cause wasting of human potentials. The objectives of this study were to determine the prevalence and associated risk factors for neonatal stunting.*

Methods: *A cross-sectional study was conducted on newborns at Tikur Anbessa Hospital from July - August 2018. Exposures were maternal socio-demographic characteristics, behavioral risk factors, and medical illnesses during pregnancy. Main outcomes were stunting defined as birth length for sex and gestational age below 3rd centiles of the INTERGROWTH-21st standard and admission to neonatal intensive care unit.*

Results: *The study included 392 singleton live births with reliable gestational age by first trimester ultrasound, last menstrual period, and Ballard scores. Stunting affected 15.1% of all newborns. In bivariate analysis, maternal socio-economic, and obstetric variables were not risk factors for stunting in a neonate, except use of biofuel for cooking ($p \leq 0.049$ 95% CI 0.586, 1.956) and parity ($p \leq 0.011$, 95% CI 1.181, 3.837). Though birth weight and birth weight for gestational age were significant factors, on multiple regression analysis only low birth weight was found to be significant determinant of neonatal stunting.*

Conclusions: *The first 1000 days post-conception is an important period to overcome intergenerational malnutrition. Prevalence of newborn stunting is high in the setting and birth weight determined stunting at birth. Further study is recommended to determine the risk factors for stunting at birth.*

Key words: *Newborn, stunting, prevalence, risk factors,*

INTRODUCTION

Undernutrition is a major public health problem that increases the global health burden of premature mortality and morbidities during childhood. According to a UNICEF report, in 2018, stunting was found to be most widespread affecting an estimated 149 million children worldwide; more than half of all stunted children under-5 more than one third lived in Africa (1). It is estimated that 45% of all deaths in children under-5 years of age are linked to malnutrition (2).

The World Health Assembly calls for 40% reduction in the prevalence of stunting in under-5 children by the year 2025 from the baseline of 2010. This implies reducing the number of stunted children from 171 million to about 100 million in 2025 (3). The national prevalence of under-five stunting is 38.4%, which is greater than the developing country average of 25% (4).

Stunting is intergenerational problem that passes on from the mother to children. Neonates with fetal growth restriction are at substantially increased risk of being stunted at 24 months and of development of some type of non-communicable diseases during adulthood (2).

Prevalence of stunting is the conventional anthropometric measure that reflects long-term chronic under-nutrition, multifactorial social deprivation, and a long-term response to the prolonged deprivation of food and/or presence of disease. Early detection of neonates who are stunted is important to take appropriate interventions at individual family level and policy making for country at large. Although stunting and its complication are rampant in developing countries, there is paucity of data on the extent of the problem in neonates. This study attempted to determine the prevalence and risk factors associated with neonatal stunting among neonates born at Tikur Anbessa Specialized Hospital.

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MATERIALS AND METHODS

Study setting

The study was conducted in obstetric department of Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa, Ethiopia. TASH is the largest referral hospital in Ethiopia with several specialties and sub-specialties. It has 800 beds capacity and serves over 300,000 patients as outpatients annually. The number of average deliveries per month is about 500 deliveries.

Study design

It is an institution based cross-sectional study conducted among neonates delivered between July and August 2018.

Study population

All neonates born during the study period at TASH were taken as source population. The study participants were all singleton live birth neonates in TASH. Neonates with following conditions were excluded from the study: all preterm less than 33 weeks, post term neonates greater than 42 weeks plus 6 days, multiple deliveries, neonates requiring urgent resuscitation and admission, and those with recognizable congenital anomalies. All neonates born to TASH during the study period were included in the study using continuous sampling.

Sample size determination

Because proportion was studied, single population proportion formula was used to calculate sample size**.**

$$N = \frac{(Z\alpha/2)^2 PQ}{E^2}$$

Because the prevalence of neonatal stunting in neonates in hospital deliveries is not known, we used P=50%, Q=50%, Z=1.96, and E=5%. Using the above formula, the sample size was 384. The final sample size was 422 after adding 10% for non-respondents.

Data collection and analysis

Gestational age was determined based on order of priority.

1) Early ultrasound before 20 weeks of gestation
2) Calculated from stated last menstrual period (LMP)
3) Estimated by Ballard's score

If the mother had early obstetric ultrasound, we took it to calculate the gestational age. If the mother didn't have early ultrasound, stated LMP was used to calculate gestational age (GA). If both are not available Ballard score was used to estimate GA. The GA was stated in weeks and days as appropriate.

Socio-demographic and clinical data were collected soon after delivery by trained data collectors. The supine newborns length was measured using Infantometer and length was recorded by centimeter with one decimal. The length was measured as early as possible after delivery within 12 hours of delivery. The length was standardized using INTERGROWTH-21st tables for gestational age and sex (5). Neonates lying below the third centile were classified as having neonatal stunting (6). The newborn weight and head circumference were also measured and standardized.

During the data collection, regular and periodic supervision was made to assure data quality and completeness.

Data analysis

After data entry and cleaning, analysis was done using the Statistical Package for Social Sciences (SPSS) version 20.0. Descriptive and analytical statistics were used as applicable. Statistically significant association was taken for *p* values <0.05. Independent variables included maternal socio-demographic data, obstetric and fetal factors. Significant factors in the bivariate analysis were subjected to multiple logistic regression analysis.

Ethical considerations

Ethical clearance was obtained from the Pediatrics and Child Health Department's Research and Publications Committee of the School of Medicine, College of Health Sciences, and Addis Ababa University. The clearance letter was submitted to obstetric department for approval. Verbal consent was obtained from parents.

RESULTS

There were a total of 422 newborns with gestational age between 33 weeks and 42 weeks and 6 days. There were 30 twin deliveries which were excluded from analysis making 392 singleton newborns as the study population.

The mean maternal age was 26.51 (SD 4.65) years, 96.41% were married and 174 (44.50%) were housewives both of which had no association with stunting. Maternal educational status, occupation and house ownership were not associated with neonatal stunting (table 1). Biofuel use as source of cooking energy was found to be significant factor for stunting ($p \leq 0.049$, 95% CI 0.59, 1.96).

Gestational age ascertainment was made using early obstetric ultrasound in 284 (72.4%) newborns, LMP in 99 (25.3%) newborns and Ballard score was used on 9 (2.3%) of newborns.

There were 190 (48.5%) male and 202 (51.5%) female newborns. Preterm newborns accounted for 43 (11.1%) while 300 (77.7 %) and 43 (11.1%) were term and post-term newborns respectively. Majority, 205 (52.3%), of the mothers were primiparous followed by multiparous 177 (45.2%) and 10 (2.6%) grand multiparous (Table 1).

The mean birth weight was 3224.04 (SD 541.2) grams and mean length was 47 (SD 2.52) centimeters. Newborn classification by birth weight showed that 331 (84.4%) were normal birth weight (NBW), 9.2% low birth weight (LBW), 6.1% macrosomic and 0.3% very low birth weight (VLBW). Majority of the newborns, 347 (88.5%), were appropriate for gestational age (AGA), 26 (6.6%) large for gestational age (LGA) and 19(4.8 %) were small for gestational age (SGA) (Table 2).

Table 1: Distribution of subjects by neonatal

Classification	Number	Percent
Classification by gestational age		
Preterm	43	11.1
Term	300	77.7
Post term	43	11.1
Total	392	100.0
Classification by birth weight		
VLBW	1	0.3
LBW	36	9.2
NBW	331	84.4
Macrosomic	24	6.1
Total	392	100.0
Classification by birth weight and gestational age		
SGA	19	4.8
AGA	347	88.5
LGA	26	6.6
Total	392	100.0

VLBW=Very low birth weight. LBW = Low birth weight. NBW = normal birth weight classification

Table 2: Parental socio-economic characteristics among study neonates

Variables	Number Births	Stunted	Not Stunted	OR (95% CI)	P Value
Maternal age (Years)					
<30	300	50	250	1.848 (0.848, 3.821)	2.396
≥ 30	90	9	81		
Maternal height (cms)					
<150	20	6	14	2.571 (0.946,6.993)	0.056
≥150-159	364	52	312		
Paternal Height (cms)					0.101
<170	176	20	156	0.612 (0.339, 1.105)	
≥170	202	35	167		
Marital status					
Married	377	57	320	1.069 (0.233, 4.902)	0.932
Not married	14	2	12		
Maternal education					
No formal education	86	15	71	1.253 (0.659, 2.389)	0.490
Formal education	305	44	261		
Maternal occupation					
Housewife	174	22	152	0.696 (0.394, 1.232)	0.212
Working	215	37	178		
Home ownership					
Self owned	55	5	50	0.522 (0.199, 1.370)	0.186
Not own	336	54	282		
Cooking fuel					
Charcoal/wood	114	18	96	1.070 (0.586, 1.956)	0.049
Gas/electricity	275	41	234		

VLBW=Very low birth weight. LBW = Low birth weight. NBW = normal birth weight
SGA= small for gestational age. AGA= Appropriate for gestational age. LGA = large for gestational age

SGA= small for gestational age. AGA= Appropriate for gestational age. LGA = large for gestational age

Parental demographic and health related factors including height, maternal age, parity, inter-pregnancy interval, pregnancy induced hypertension and anemia during pregnancy did not show significant association with stunting. Only 49 (12.5%) of the mother had medical conditions.

Of these, 33 (8.4%) had pregnancy induced hypertension (PIH); among the the rest, five (1.3%) maternal diabetes, three (0.8%) cardiac illnesses, two (0.5%) HIV/AIDS, three (0.8%) thyrotoxicosis, and three (0.8%) had other diseases. Anemia in pregnancy and iron supplementation did not show significant relation with stunting (table 2, 3).

More than two-third (68.4%) of newborns who were SGA were stunted compared to only 12.4% of AGA and LGA. Newborns born to primiparous mothers were twice more affected than multiparous mothers 19.4 % against 10.2% ($p \leq 0.011$, 95% CI 1.181, 3.837) (table 3). Prevalence of newborn stunting was 21.2% among mothers with PIH compared to 14.8% among mothers without PIH (p=0.304).

Infant sex and gestational age did not show significant relation with stunting; however, weight for gestational age and LBW were found to be significant factors for stunting in bivariate analysis (table 3). However, on multiple logistic regressions, only LBW was found to be a predictor of stunting in newborns at birth ($p \leq 0.001$, 95% CI 0.027,0.194).

Table 3: Maternal obstetric and fetal factors for stunting among neonates at birth

Variables	No. births	Stunted	Not Stunted	OR (95%CI)	P value
Maternal PIH					
Yes	33	7	26	1.584 (0.654, 3.838)	0.304
No	358	52	306		
Parity					
Primiparous	201	39	162	2.129 (1.81,3.837)	0.011
Multi/grand multiparous	187	19	168		
Inter-pregnancy interval					
<24 months	51	6	45	1.125 (0.415, 3.049)	0.817
≥24months	151	16	135		
Gestational age					
Preterm	43	9	34	1.546 (0.699, 3.419)	0.279
Term/Post-term	342	50	292		
Birth weight for GA					
SGA	19	13	6	15.365 (5.562, 42.387)	0.000
AGA/LGA	372	46	326		
Maternal hemoglobin (gm/dl)					0.406
<11	18	4	14	1.621 (0.513, 5.117)	
≥11	347	52	295		
Iron supplementation					
< 3 months	269	34	235	0.689 (0.365, 1.300)	0.249
> 3 months	98	17	81		
Sex of neonate					
Male	188	32	156	1.337 (0.767, 2.331)	0.304
Female	203	27	176		
Birth weight					
LBW	37	24	13	16.826 (7.87, 35.97)	0.000
Not LBW	354	35	319		

Although multiple pregnancies were excluded from final analysis, the 30 twin deliveries during the study period were analyzed. Using the same curves for the 30 twins, 15 (50%) were stunted; more than 5.6-fold risk of being stunted as compared to singletons where the rate of stunting was 15% (OR was 5.64, 95%CI 2.52-12.15) *P value <0.01* (table 4).

Table 4: Comparison of prevalence of stunting singleton and twin deliveries at birth

Deliveries	Total number	Stunted	Not stunted	OR (95%CI)	P value
Singleton	392	59	333	1 (Reference)	<0.01
Twin	30	15	15	5.64 (2.62-12.15)	

DISCUSSIONS

Recent estimates suggest that stunting, wasting, and intrauterine growth restriction are responsible for 2.2 million deaths and 21% of disability-adjusted life years lost among children younger than 5 years (7). Until recently, the idea that newborns also get stunted was non-existent.

Stunting is a cumulative process, often apparent by birth but worsening until around the age of 2 years when growth becomes canalized (8). It was noted by an earlier study that height-for-age at 2 years was the best predictor of human capital and that undernutrition is associated with lower human capital (9). In this study, it has been attempted to determine the extent of stunting of neonates at birth and its determinants.

There are few data on the extent of stunting at birth; most of the studies focused on under-five children. Recently, a study on newborn stunting at birth was published from Gondar, Ethiopia (9). However, the Gondar study used 10th percentile as a cut-off for defining stunting as opposed to 3rd centile in this study.
In this study, the prevalence of stunting was higher than the finding in a previous study where multinational study from eight centers in the world found prevalence of stunting of 3.8% (6) and 6.5% in Brazil using the INTERGROWTH-21st and BRISA chart (11). This may be expected because the previous study was done among high, middle, and low income countries to develop the centile curves for newborn standardization.

On the other hand, the prevalence of stunting at birth is lower than the 30% of Gondar study (10) which is probably due to the difference in the cut-off for stunting and that of study in Guatemala which was 33% (12). The difference from the Guatemalan study is that it included all infants up to 6 weeks of age and also used a different criterion. Even though it is smaller than the two studies mentioned above, the high rate in Ethiopia, Addis Ababa is very much concerning to address as it might lead to huge economic and social burden on an already deprived society.

A number of maternal, fetal, and placental factors are known to affect the growth of the fetus. In this study, none of the socioeconomic factors significantly affected stunting in a neonate at birth. Earlier, it was shown that socioeconomic factors (income, education, and occupation) appeared to be of little importance as determinants of growth (13). In this study, biofuel use for cooking has been found a significant factor for stunting at birth.

In developing countries, most mothers depend on biofuel especially in rural settings. Indoor air pollution from solid fuel use is a confirmed risk factor for acute lower respiratory tract infections, especially in children in developing countries (14). Earlier studies have found association of biofuel pollution to affect birth outcomes (15,16) but not in the Gondar study (10). This study has shown that biofuels are harmful to the fetus as well.

In this study, maternal factors such as stature and age were not identified as factors for stunting. Other studies found that short maternal stature and young age affects length (6,10) and it is an important determinant of intrauterine growth restriction and low birth weight, especially in developing countries (17). In a study that examined the association between maternal stature and offspring mortality, underweight, stunting, and wasting in infancy and early childhood in 54 low- to middle-income countries a 1-cm increase in height was associated with a decreased risk in stunting (RR,0.968;95%CI,0.967-0.968) (18). This discordance with our results requires further study for further interventions to curb the intergenerational malnutrition.

This study has attempted to identify fetal factors associated with stunting. Sex of the neonate does not seem to affect stunting in newborns similar to what has been found earlier in among under-five children. However, study from Gondar found that males were more at risk of stunting at birth than females (10).

At the moment from these studies, no apparent reason for discordance in the report and the sex as a risk factor. Weight for gestational age and birth weight were found to be associated factors in bivariate analysis but when subjected to multiple logistic regression, only low birth weight was found as significant risk factor (95% CI 0.027, 0.194) in concordance to the Gondar study (10).

The strength of the study is that it used recently developed standards for fetal growth restriction to explain fetal growth restriction beyond sole reliance on birth weight. In addition, it is among few studies that determined stunting at birth. Possible limitation of the study is that included hospital deliveries where most maternal illness were few especially chronic diseases which might affect fetal growth.

In conclusion, prevalence of newborn stunting was 15.1% in neonates born at Tikur Anbessa Specialized Hospital. We recommend to measure length at birth and standardize the length using newborn growth standards to identify the stunted newborns to deliver appropriate health interventions to halt the long-term consequences of newborn stunting.

Furthermore, identification of the risk factors for stunting at birth is required with a larger sample size. To avert the high rate of stunting, there is a need for prenatal and early-life interventions to prevent the growth failure that mainly happens during the first 2 years of life, including the promotion of appropriate infant feeding practices as it has been proposed (19).

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Conflict of interest
None

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ORIGINAL ARTICLE

KNOWLEDGE, ATTITUDE AND PRACTICES OF PARENTS AND GUARDIANS OF CHILDREN WITH EPILEPSY AT PEDIATRIC NEUROLOGY CLINIC OF TIKUR ANBESSA SPECIALIZED HOSPITAL. ADDIS ABABA, ETHIOPIA

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ABSTRACT

Introduction: *Epilepsy is considered to be present when 2 or more unprovoked seizures occur in a time frame of longer than 24 hr. Public awareness and attitudes towards epilepsy differ across cultures. It has been noted that traditional beliefs and lack of knowledge strongly influence attitudes towards epilepsy. Epilepsy remains a stigmatized disease especially in Sub-Saharan Africa.*

Objectives: *To assess knowledge, attitude and practices of parents and guardians of children with epilepsy attending follow up at pediatric neurology clinic in Tikur Anbessa Specialized Hospital.*

Methods: *A hospital based cross-sectional descriptive study was conducted among 186 parents and guardians of children with epilepsy attending pediatrics neurology clinic from September 1 to October 30, 2018.*

Results: *More than 138(60%) of the parents/guardians had some knowledge on the type of antiepileptic drug treatment their children were receiving and 67(36%) of parents/guardian know the type of illness they suffering from. Fifty-eight percent of the parents/guardians administered some recommended first aid measures to their epileptic children during a fit, but many of them combined these with potentially harmful first aid measures. Spiritual healing and to a lesser extent traditional medicine were perceived to be important components of therapy for epilepsy when used in conjunction with hospital treatment. An increased level of education of the parents/guardians had a positive influence on their knowledge, attitudes and practices towards epilepsy.*

Conclusions: *Overall parental attitude seems to be more positive. Even though there were encouraging results on the parental knowledge there is still a gap that can cause misconception on the practice. Ensuring education and support at community and school levels for both parents and children with epilepsy should be the principal goal of health-care service.*

Key words: *Epilepsy, Knowledge, Attitude, Practice, Children, Ethiopia*

INTRODUCTION

Epilepsy is two or more unprovoked seizures unrelated to acute metabolic disorders or withdrawal of drugs or alcohol. It is characterized by a tendency to recurrent unprovoked seizures which can lead to loss of awareness or consciousness, disturbances of movement, sensation (including vision, hearing, and taste), autonomic function, mood, and mental function (1, 2).

Epilepsy is a common chronic neurological disorder of considerable public health importance. Approximately 50 million people worldwide have epilepsy, making it one of the most common neurological diseases globally. Nearly 80% of the people with epilepsy live in low- and middle-income countries (2).

The main reasons for a higher incidence of epilepsy in developing countries are the higher risk of acute and chronic brain infections, pre- and post-natal obstetric complications leading to brain damage (1).

The median incidence of acute symptomatic seizures is 29–39 per 100,000 per year. Acute symptomatic seizures predominate in the youngest age class (under1 year of age) and in the elderly. The pooled incidence rate of epilepsy was 61.4 per 100,000 person-years. The incidence was higher in low/middle-income countries than in high-income countries(3). The prevalence of epilepsies in childhood and adolescence is 4-6 per 1000. The peak prevalence is in the 1-4-year age range (1). In a large community-based study, the prevalence of epilepsy in Ethiopia was reported to be 5.2/1000 population (4).

Public awareness and attitudes towards epilepsy differ across cultures. It has been noted that traditional beliefs and lack of knowledge strongly influence attitudes towards epilepsy. Epilepsy in children has wide repercussions on social, emotional, and overall family functioning, particularly in families where younger children are affected and in those with single parents (5).

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Epilepsy remains a stigmatized disease, especially in Sub-Saharan Africa. Lack of information and illiteracy has been blamed as the cause of the stigmatization. This Stigmatization stems from the fact that the traditional African belief views epilepsy as a spiritual disease (6).

Epilepsy is the commonest neurological condition seen in children's outpatient clinics in TASH pediatrics neurology outpatient clinic (7). It is a treatable condition in the majority of patients, yet majority of our epileptic patients are untreated. Inappropriate attitude, and lack of knowledge regarding epilepsy have been shown to significantly influence the size of the treatment gap and the level of compliance to treatment. It is also being associated with increased morbidity and mortality (1). So far, the information gathered on knowledge, attitude and practice regarding epilepsy has been on the general community in people not necessarily having epilepsy and those who may not necessarily have taken care of an epileptic person. Despite the high burden of epilepsy to our knowledge no research is done on assessment of parental knowledge and attitude toward child with epilepsy in our set up.

MATERIALS AND METHODS

Study setting

The study was conducted at the pediatrics neurologic clinic of Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia. The hospital is the largest teaching hospital and tertiary referral hospital in the country providing undergraduate as well as post graduate teaching service. The pediatric neurology clinic works in all of the five working days. It is run by trained nurses, Pediatric and Child Health Residents, and a pediatric neurologist. It is attended by children and adolescents in the age ranges of 0-18 years. The average number of patients attending the clinic on daily basis is around 30.

Study Population

All parents or guardians of children with a clinical diagnosis of epilepsy attending neurology clinic at TASH during the study period were eligible for the study.

Study Design

The study was a hospital based cross-sectional descriptive study conducted from September 1 to October 30, 2018.

Sample size

The sample size was calculated using Leslie Fishers formula

$n = Z^2P\ (1\text{-}P)/\ d^2$

Where: n is the sample size, z = 1.96 (normal distribution curve). P is the expected prevalence = 50%, as there has not been a published study done regarding KAP of parents and guardians of children with epilepsy at TASH before.

d is the error of the estimate (absolute precision) (±5%); with 95% confidence level.

$n= 1.96^2 \times 0.5\ (0.5)/\ 0.05^2 = 384$

Sample size correction for finite population is valid to be used for sample sizes with proportion greater than 5% of the source population (i.e. n/ N>0.05). Our source population was 300.

$$n' = \frac{NZ^2P(1-P)}{d^2(N-1) + Z^2P(1-P)}$$

Where n, = sample size with finite population correction

N= population size (300)

The corrected sample using EPI info statistical package for sample size was 169.Taking an additional 10% non-responder, **186** patients were included in the study.

Sampling Technique

Convenience sampling technique was used .

Operational Definition

Stigma is defined as any social attribute that is deeply discrediting for an individual and, in the case of epilepsy, it can significantly affect the health-related quality of life of the patients in many everyday activities such as going to school, working, driving and creating a family.

A seizure is defined as a transient occurrence of signs and/or symptoms resulting from abnormal excessive or synchronous neuronal activity in the brain (3, 12).

Epilepsy is defined as two or more unprovoked seizures that occur in a time frame of longer than 24 hours.

Data collection, quality, data analysis and statistical methods

A structured questionnaire was designed by extrapolating from reviewed literatures for the study. It comprises 5 sections: parental socio demographic characteristics, demographic and clinical characteristics of children with epilepsy, knowledge, attitude and practices related to epilepsy. Data collectors were 3 nurses recruited from neurology clinic and trained on how to fill the questionnaire. Piloting of the questionnaire was done among 10% of the intended sample size. Data were entered, cleaned and analyzed using SPSS version 24. Descriptive and analytical statistics was used as applicable. Statistically significant association was taken for p values of <0.05.

Ethical Consideration

Ethical clearance was obtained from the Pediatrics and Child Health Department's Research and Publications Committee of the School of Medicine, College of Health Sciences, and Addis Ababa University. Respondents were clearly informed about the purpose of the study and the information required from them

Participant confidentiality was assured. Patients who refuse to take part in the study received the same quality of health care service as the participants. All participants included in the study were kept anonymous.

RESULTS

Socio-demographic characteristics

More than half of the children115 (61.8%) were males. The mean age was 8.4 years with standard deviation of 4. 6 years. The commonest type of seizure recorded was generalized tonic-clonic type 154 (78.6%). About 61(32.8%) of children had been on treatment for a period of 2-4years followed by 58 (31.2%) >6years. Half 94(50.5%) of patient had good control of seizure with the remaining patients with fair and poor control.

Majority of the respondent parents/guardians were mothers 105(56.5%). Most of the parents/guardians 88 (47.3%) were 30-39 years old and 84(45.2%) of them attended secondary school. Majority of our patients are from Addis Ababa. A significant proportion of parents/guardians 118(63.5%) are unemployed and for 65(43%) of parents /guardians their income is less than 2000birr per month.

Knowledge assessment of parents /guardian: Each parent/guardian was asked to mention the type of illness his/her child was suffering from and only 67 (36%) of parents know the terminology 'epilepsy'. Forty eight percent of the parents/guardians said they did not know what causes epilepsy.

The commonest causes of epilepsy mentioned by the others were head injury 33(17.7%) followed in order by perinatal events 30(16.6%), infection 15 (8.1%) and evil spirit 11(5.9%).

The knowledge on features of convulsion and the type of drugs their children taking was presented on Table 1. The commonest mentioned feature being jerky movement of the limbs.

Majority 159(85.5%) of the parents/guardian said epilepsy is not contagious, 24(12.9%) said they did not know, and 3(1.6%) said that it can be contagious. For more than half of the parents 117 (57.9%), their primary source of information for epilepsy was medical doctor (Table2).

Table 1: Knowledge on the current antiepileptic drug treatment and features of convulsion among 186 parents/ guardian of epileptic children at Tikur Anbessa Specialized Hospital, 2018

Variables	**Frequency**	**Percent**
Antiepileptic drug (n=225)		
Phenobarbital	42	18.7
Phenytoin	51	22.7
Valporic acid	34	15.1
Carbamazepine	10	4.4
Clonazepam	1	0.4
Other	1	0.4
Don't know	86	38.2
Knowledge on the features of a convulsion (n=288)		
Jerky' limb movements	104	36.1
Rolling of the eyes	18	6.3
Loss of consciousness	25	8.7
Urine/stool incontinence	10	3.5
Frothing/drooling of saliva	35	12.2
Stiffening of the limps	29	10.1
Staring gaze	6	2.1
Closing of the eyes	5	1.7
Child falls to the ground	2	0.7
Twitching of the eyes	22	7.6
Twitching of the mouth	8	2.8
Falls asleep	3	1.0
Staggering gate	3	1.0
Weakness	1	0.3
Aggressiveness	3	1.0
Biting the tongue	3	1.0
Don't know	11	3.8

Table 2: Distribution of knowledge on transmission of epilepsy and curability and type of care given to an epileptic child during a fit

Variables	Frequency	Percent
Epilepsy transmitted		
Yes	3	1.6
No	159	85.5
Don't know	24	12.9
Curable		
Yes	141	75.8
no	14	7.5
don't know	31	16.7
Source of information		
Radio/TV	9	4.5
Community	69	34.2
Health profession	117	57.9
Other	7	3.5
The type of care given to an epileptic child during convulsion		
Put spoon/finger in the mouth	19	9.8
Hold the child to avoid falling	19	9.8
Loosen tight clothes	8	4.1
Stay with the child till convulsion is over	24	12.4
Hold the child for comfort	24	12.4
Hold to restrict movements	2	1.0
Remove harmful objects around the child	14	7.3
Put to lie on the side	11	5.7
Put child to lie on the back	7	3.6
Support the head with something soft	12	6.2
Give a cold drink	9	4.7
Wipe with wet cloth	33	17.1
No first aid measures	5	2.6
Other	6	3.1

Bivariate analysis of socio-demographic characterstics of parents with their knowledge: Those parents/ guardians who have government job and those with higher income >4000 had an appropriate knowledge with (P =0.04). Parents/guardians with secondary school educational level and higher (38.5%) were more likely to mention head injury as a cause of epilepsy compared to those with below secondary school educational level (10.7% and 14.3% respectively). (P = 0.00). A significantly higher proportion of the parents/guardians with secondary school education and below (56% and 52.4% respectively) did not know the causes of epilepsy (P = 0.01) (Table 3).

Assessment of parents/guardian practices during epilepsy

The first aid measures administered by many of the parents/'guardians 33(17.1%) wiping with wet cloth followed by those who stay with their child till the convulsion was over 24(12.4%), holding for comfort 24(12.4%) and 19(9.8%) put spoon/finger in the mouth.

Majority of parents/'guardians 108(57.9%) administered at least one recommended first aid measure, however significant number of parents/guardians 42.1% combined recommended first ai measures with unnecessary, and potentially harmful and harmful first aid measures.

A statistically significant higher proportion of parents/guardians with post-secondary school education stay with their children till convulsion is over 20.5% and also remove harmful objects around the child compared to parents/guardians with secondary school education and below (P = 0.03 and 0.04 respectively).

About 38.1% of parents/guardian who attend primary school or below don't give any first aid measure (P=0.01) (Table 2).

Table 3: Distribution of knowledge on the type of illness, perceived causes of epilepsy and antiepileptic drug treatment by educational level and income of parents/guardians

Variables	Total	Knowledge of type of illness Appropriate (%)	Inappropriate (%)	Chi square	p-value
Job					
Government	43	26(60.5)	17(39.5)	6.5	0.04
Private	25	12(48.0)	13(52.0)		
Unemployed	118	45(38.1)	73(61.9)		
Monthly income					
<2000	65	27(41.5)	38(58.5)	6.3	0.04
2000-4000	49	20(40.8)	29(29.2)		
>4000	37	24(64.9)	13(35.1)		
Variables	Total no	Knowledge of Drug Appropriate (%)	Inappropriate (%)	Chi square	p-value
Educational status of parents					
Primary school and below					
Secondary school	63	25(39.7)	38(60.3)	15.5	0.00
Above secondary	84	44(52.4)	40(47.6)		
	39	31(79.5)	8(20.5)		
Monthly income					
<2000	65	34(52.3)	31(47.7)	7.7	0.02
2000-4000	49	26(53.1)	23(46.9)		
>4000	37	29(78.4)	8(21.6)		
Cause	Educational status			Chi square	p-value
	Primary and below 63	Secondary 70	Above secondary 34		
Head injury	14.3	10.7	38.5	14.8	0.00
Infection	4.8	10.7	7.7	1.7	0.42
Perinatal event	15.9	15.5	20.5	0.53	0.77
Others	14.3	7.1	5.1	3.2	0.21
Don't know	52.4	56.0	28.2	8.7	0.01

Parents' attitudes towards their children's epilepsy:

The attitude of parents is shown in **Table 4**. The strongest positive attitude was obtained for the assertion "I want my family and friends to know that my child is suffering from epilepsy" in 161(86.6%).

On the contrary, the least positive attitude was observed for the assertion most parents felt that the child will not achieve a lot in the future, and they treated him/her differently, and 122 (65.6 %) felt that epileptic patients should work in special job and with each other.

Table 4: Attitude of parents towards epilepsy

Variables	Frequency	Percent
Do you want your family and friends to know that your child is suffering from epilepsy?		
Yes	161	86.6
No	25	13.4
Do you feel that other people treat your child as less valuable?		
Yes	88	47.4
No	89	47.8
Don't know	9	4.8
Do you think that your child will be able to achieve professional success later in life?		
Yes	150	80.6
No	36	19.4
Do you have a concern that your child has problems making friends?	81	43.5
Yes	105	56.5
No		
Yes	139	74.7
No	47	25.3
The intelligence of epileptic persons is lower than normal persons		
Yes	108	58.1
No	78	41.9
Epileptic patients should work in special jobs and with each other		
Yes	122	65.6
. No	64	34.4
Could the child with epilepsy get married in the future?	154	82.8
Yes	32	17.2
No		

DISCUSSION

The important causes of epilepsy in developing countries are acute and chronic brain infections, pre- and post-natal obstetric complications (1). In this study most of the parents/guardians (43.5%) knew of at least one possible cause of epilepsy. This is better than what was found by Levy' in Zimbabwe <1% and Tekle- Haimanot et al in Ethiopia where 6% parents knew of at least one cause of epilepsy. This result was attributed to the fact that most of parents included in this study live in the urban set-up and 84% have primary education and above unlike the above studies which was done at rural set-up (8, 9).

Only 5.9% of the parents/guardians in this study ascribed epilepsy to supernatural causes as evil spirit. Such misconceptions can have significant negative implications on the medical management with a higher risk of non-compliance (1, 8-11). The finding in this study is better than Muasya CK, in Kenya where 12% of parents attributed epilepsy to supernatural causes. Even though both studies were done in urban setup, most of the study participants in the later study had educational level below secondary school (1).

A few numbers of parents/guardians (1.6%) thought that epilepsy is contagious. These finding is also better than what was found by Tekle-Haimanot et al in Ethiopia and other studies done in Africa and Asia where many of the respondents thought that epilepsy was contagious. The notion that epilepsy is contagious by direct physical contact during an attack is the base of stigmatization of these patients (1, 5, 9, 12,13).

Almost all the parents/guardians (96.2%) recognized at least one feature of a convulsion. The most frequently recognized features were Jerky' limb movements, frothing/drooling of saliva and Stiffening of the limps which are common manifestations of a GTCS, the commonest reported seizure type in this study and in many other published reports (1,9). This showed that parents notice only those with obvious motor activity to have a seizure, other types of seizures are not known by many parents. It is therefore important to recognize the features of a convulsion in order to act fast and avoid complications which may result from a poorly managed convulsion.

Fifty-eight percent of parents/guardian administered at least one recommended first aid measure to their epileptic children during a fit. But many, combine this with potentially harmful and harmful first aid measures. The overall effect of such combinations was at times more harmful than useful to the child. These practices, however, were better than the one found by Al. Zubaidi et al in Jeddah and Tekle-Haimanot et al in Ethiopia where 31.1% and 11% of the respondents respectively knew of some recommended care to give to an epileptic person during a fit (9, 13).

A small number of parents/guardians (2.6%) in this study did not administer any first aid measure to their epileptic children during a fit. The reasons given in order where they take the child to health facility and the convulsions were usually very brief. This is, in contrast to study done in Kenya where many did not administer first aid because they did not know the type of first aid to be administered to a convulsing child. Other studies done in Ethiopia revealed that many people did not attempt to assist an epileptic person during a fit in fear that they would contract the disease (1, 8, 10).

Majority of the parents/guardians in this study 66.2% had only used hospital treatment for managing their epileptic children. All the rest 33.8% combined hospital treatment with spiritual healing, and a few of them also used traditional medicine. These findings suggest that many parents/ guardians perceived some continuing benefits from alternative methods of treatment, even though they continued to seek "modern" medicine. It is higher than found in Kenya 18.2%. Similar findings were also found in other studies done in Africa (1, 9, 11).

Majority of the parents in this study had positive attitude in contrast to the findings revealed by Dung-Dung et al and Al. Zubaidi et al (12,13). which was predominantly negative. This was attributed to the fact that most parents want to share their child's illness with their families and relatives. This also indicates that parents had felt less stigmatized due to their child's epilepsy. Specifically, fear of discrimination and social stigmatization represent major problems both for children with epilepsy and for their parents.

On the other hand, there was negative attitude among the parents pertaining to academic performance and intelligence. Epilepsy was also regarded as an obstacle for a successful life. These findings were consistent with what was found in Jeddah by Al. Zubaidi et al where 84.4% of parents agreed that epilepsy is an obstacle for a good life (13).

Conclusion

In conclusion, parental knowledge and practice requires improvement in some epilepsy-related issues. Although parents encounter challenges at various levels, overall parental attitudes seem to be more positive. An increased level of education had a positive influence on KAP towards epilepsy. We recommend more effort by the health sector to ensure education and support at the community and school levels for both parents and children with epilepsy.

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Conflict of Interest

Authors have no conflict of interest to declare.

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ORIGINAL ARTICLE

CLINICAL OUTCOMES OF ADOLESCENTS LIVING WITH HIV AFTER TRANSFER TO ADULT CARE IN A TERTIARY HOSPITAL, ETHIOPIA: A RETROSPECTIVE OBSERVATIONAL STUDY

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ABSTRACT

Introduction*: Transferring adolescents living with HIV to adult care is beyond changing the services location. The transition process will significantly affect the success of antiretroviral therapy (ART) for individual patients and the overall HIV program in a country. This study assessed the clinical outcomes of adolescents living with HIV who were transferred to adult care in Addis Ababa, Ethiopia.*

Methods*: A facility-based retrospective observational study was conducted at a tertiary care hospital. Data collection was based on a review of the clinical records of adolescents living with HIV that were transferred from pediatric to adult ART clinic. Data was extracted from paper-based and electronic medical records of patients seen from January 2016 to December 31, 2017, using a structured data extraction tool. The data were analyzed using SPSS version 24.*

Result*: Out of the 151 adolescents included in this study, 18 (11.9%) were lost to follow up (LTFU) after one year of transfer to adult care. There was one death, which occurred three months after the transfer. At the time of transfer, 11(7.4%) of the adolescents had fair or poor adherence to treatment recommendations, and after six months of the transfer, this number increased to 52(34.7%). In addition, the percentages of adolescents with CD4 count< 200 cells/mm^3 increased from 2.6% at the time of transfer to 6.7 % six months after transfer. This represented a statistically significant decrease in the mean CD4 count of 50 (13.3 vs 86.9, p=0.008).*

Conclusions*: Although the majority of adolescents remained engaged in their follow-up after transfer to adult care, there was a significant gap in adherence to their treatment. These are also reflected by a subsequent increment of adolescents with a CD4 count of less than 200 cells/µl. Thus, more should be done to ease the adolescents' transition process and improve their adherence.*

Keywords*: Adolescents, Antiretroviral, HIV, Transition, Lost to follow up*

INTRODUCTION

Adolescents living with HIV (ALHIV) are enrolled in HIV care, mostly in pediatric clinical settings. When they grow into adulthood, they need to be transferred from pediatric to adult care. Healthcare transition (HCT) does not merely change location from pediatrics to adult clinics; instead, it is a planned and purposeful transition of adolescents to engage them in their health and disease management meaningfully (1). The success of the transition process significantly affects the success of antiretroviral treatment (ART) for individual patients as well as for the overall HIV program in a country (2). However, this transition can be difficult due to potential barriers.

HCT from pediatrics to adult care is challenging for several reasons. For example, fear of disrupting the relationship between the patient and the health care provider in pediatric care emphasizes the need for youth-friendly services (1-4).

The presence of HIV makes this process more complicated due to associated psychosocial and developmental problems and comorbidities in the context of coping with a chronic, potentially stigmatizing disease (3,4). Adolescents and young adults living with HIV are also highly vulnerable to depression (4,5). In addition, they may deny their HIV status (6) and are prone to risk-taking (7), which may lead them to higher risks of HIV transmission, treatment interruption, adherence problems, treatment failure, and loss to follow-up (2). These issues may be more pertinent for prenatally infected adolescents compared to behaviorally infected adolescents (8).

ART has been successful in reducing mortality among people living with HIV AIDS (PLWHA). However, improvements among adolescents and young adults have been less pronounced than among children and adults (9).

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Results from retrospective cohort studies in North America have shown that poor adherence and loss to follow-up (LTFU) are common after transfer to adult care (10,11). Although CD4 count >500 cells/mm^3 (10) and retention rates (11) were initially high, these declined significantly by the second year after transition. Both samples were small and done in resource-rich countries, where population characteristics and health systems are different from those found in Low and Middle-Income Countries (LMIC). A study with a large sample from Kenya was also consistent with these findings, demonstrating higher LTFU among youth than other age groups (12). Our study focused on assessing the clinical outcomes of adolescents living with HIV after the transition to adult services in TASH, where there are no specialist services for adolescents (13). Findings will have the potential to inform the development of appropriate services for this age group in this setting and other similar settings in LMIC.

METHODS

Setting

Tikur Anbessa Specialized Hospital (TASH), where this study was conducted, is the largest teaching hospital in Ethiopia, with over 700 beds, and offers diagnosis and treatment to over 400,000 patients a year. Pediatric Infectious Diseases Clinic (PIDC) gives comprehensive care and treatment for over 300 children per month. It is staffed with one consultant specialist on pediatric infectious diseases, one fellow in pediatric infectious diseases, one to two residents, one general practitioner (GP), and five nurses. Adult ART clinic is a separate clinic that evaluates over 3000 adults per month and has no separate clinic for adolescents at the time of the study. It is staffed with two consultant specialists on infectious diseases, one to three residents, and eight nurses. Both PIDC and adult ART clinics give service five days per week during office hours and half days during weekends.

The transition process

TASH pediatric patients with HIV are followed in the PIDC and transferred to adult ART clinics when they reach at least 16 years of age, or whenever the staff thinks they are ready to be transferred. The adult ART clinic is found in the same compound, and patients get transferred along with their complete paper-based medical follow-up chart, and follow-up would continue with the same medical follow-up chart at the adult ART clinic. At the time of the study, there was no separate transition service or adolescent clinic with its guideline in the hospital to facilitate care transfer.

Study design and period

An institution-based retrospective observational study was conducted in adolescents living with HIV transferred into adult ART clinics from January 2016 to December 31, 2017.

Sample size determination

The sample size calculated using the single population proportion formula, $n=Z^2*P\ (1-P)/d^2$ and adjusted sample size (n) = (N*n)/(N+n), where Z=1.96 for 95% confidence interval, P=24%, taken from another study reporting lost to follow up rate (10),and "d" is the desired precision (0.05). N is the finite population estimated to be 330 at the time of data collection. The adjusted final sample size was found to be 151.

Study population and sampling

Clinical records were reviewed to identify adolescents living with HIV transferred from PIDC to adult ART clinics. The study population was all adolescents who were attending adult clinics and fulfilling the inclusion criteria (those engaged in care in pediatric care before the transfer, and elapsed time of at least one year since the transfer) were included. Adolescents living with HIV who were directly linked to the adult ART clinics (has not been in pediatric clinic), and elapsed time of less than one year since transfer were excluded.

Study variables

The primary outcome variables were LTFU, adherence to their current drug regimen, immunological response, treatment failure, and mortality.

Definitions

Age groups:

In this study, the definitions used for adolescents (age 10-19 years) and youth (10-24 years) were similar to those used in the literature (14)

The formal transition of adolescents living with HIV was defined as the "purposeful, planned movement of adolescents with chronic physical and medical conditions from child-centered to adult-oriented health care systems"(15)

Functional status is defined as:

1. Working: If they can perform everyday work in and out of the house.
2. Ambulatory: If they can perform activities for daily living.
3. Bedridden: Individuals not able to perform activities of daily living.

Lost to follow up (LTFU): Has not visited health care or follow up for more than six months (15,16).

Engaged in care: Visited health care on their appointment within the past three to six months (15, 16).

Good adherence: If they took more than 95% of their medication or missed <2 doses per month.

Fair adherence*:* If they took 85-94% of their medication or missed 3-5 doses per month.
Poor Adherence: If they took less than 85% of their medication or missed >5 doses per month.

Treatment failure: After six months of treatment if there is one or all of the following (15, 16).

1. New or recurrent clinical events indicating severe immunodeficiency.
2. CD4 count falls to the baseline (or below) or persistent CD4 levels below 100 cells/mm^3.
3. Plasma viral load above 1000 copies/ ml.

Data collection

The data extraction form was adopted from the ART intake form, follow-up form, and after reviewing similar literature (10,11). The checklist was prepared in English and had four parts. It contained socio-demographic questions, clinical data, adherence to the ART, and clinical outcomes. Data were abstracted at different time points; at the start of ART, at transfer, six months post-transfer, one year post-transfer. Two nurses collected the data after one day of training on the structured checklist and collection techniques. The principal investigator supervised the data collecting process.

Data analysis

Data were cleaned before entry. Then it was coded and entered into SPSS version 24 for analysis and descriptive statistics. Descriptive statics (proportion, percentage, ratio, frequency distribution, central tendency, and measure of dispersion) and tabular presentation were used to summarize the data. Paired-t-test was used to compare pre-and post-transition CD4 count.

Ethical considerations

Ethical clearance was obtained from the Department Research and Publication Committee (DRPC) of the Department of Pediatrics and Child Health, College of Health Sciences, Addis Ababa University. No personal identifier information was included in the study.

RESULTS

One hundred fifty-one adolescents were transferred from PIDC to adult ART clinics during the study period. Out of the 151 adolescents, 87 (57.6%) were male. The median (interquartile range [IQR]) duration of stay at PIDC was 10 (IQR 9, 11) years. The median age at diagnosis of HIV was 8 (IQR 7, 10) years and the median age at transfer was 18 (IQR 17, 19) years. The median age at the time of data collection was 20 (IQR 19, 21) years, with the median duration of stay at adult ART clinic follow-up was two years (IQR 2, 2)**(**Table 1).

Table 1: Socio-demographic Characteristics of Adolescents Living with HIV in 2016/2017 at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia

Variable	n (%) or median (IQR)
Gender	
Male	87 (57.6)
Female	64 (42.4)
Age at diagnosis	8 (7.10)
Age at start of ART	
Less than 18 months	1 (0.7)
18 to 59 months	1(0.7)
60 months to 120 months	114 (75.5)
Above 120 months	35 (23.2)
Age at transfer to adult clinic	18 (17.19)
Current age	20 (19.21)
Age at disclosure	12 (11, 14)
Duration of stay at pediatric	10 (9.11)
Duration of stay at adult care	2 (2, 2)

One hundred thirty-two (87.4%) remained engaged in care after one year of transfer to adult care. Eighteen (11.9%) were lost from follow-up (LTFU); two of them were LTFU within six months of transfer and 16 within one year of transfer. One death occurred three months after the transfer, and the cause of death was respiratory failure secondary to ARDS.

Adherence

Eleven (7.4%) of the adolescents had fair or poor adherence at the time of transfer, and six months post-transfer, this number has increased to 52(34.7%). At one year of transfer, the rate of poor or fair adherence was 33(22.0%), slightly lower than six months post-transfer.

Medical outcomes

At the time of transfer, 73(48.3%) adolescents had a CD4 count above 500 cells/µl, 50(33.1%) between 200 cells/µl and 500 cells/µl, only 4(2.6%) were having severe immune-compromised with a CD4 count below 200 cells/µl, and the rest 24(15.9%) patients had unknown CD4 count. This changed at six months of post-transfer, with an increase in the proportion of adolescents with CD4 count < 200 cells/µl was 10(6.7%). This represented a statistically significant decrease in the mean CD4 count of 50 (13.3 vs86.9, p=0.008). A one-year post-transfer CD4 count was done only for 13 adolescents, making it challenging to analyze. Viral load was done only for a few patients, so there was inadequate data to make comparisons. ART regimen changed to 24(15.9%) adolescents post-transfer, of whom 18 were due to treatment failure. There was no difference in WHO clinical staging, functional status, and weight pre and post-transfer (Table 2).

Table 2: Pre and post-transition Outcomes of Adolescents Living with HIV in 2016/2017 at Tikur Anbessa Specialized Hospital, Addis Ababa

Variables	At start of ART	At transfer	At 6month of transfer	At 1 year of transfer
	n (%)	n (%)	n (%)	n (%)
WHO clinical stage				
Stage I	5 (3.3)	144 (95.4)	143 (95.3)	142 (94.7)
Stages II,III, IV	146 (96.7)	7(4.6)	7(4.7)	8(5.3)
CD4 (cells/mm^3)				
Below 200	51 (33.8)	4 (2.6)	10 (6.7)	0(0)
>200	91 (60.2)	123(81.5)	65 (43.3)	13(8.7)
Unknown	9(6.0)	24(15.9)	75(49.7)	137(91.3)
Viral load copies/µl				
Undetectable	**0**(0)	6 (4.0)	14 (9.3)	11 (7.3)
Detectable	0(0)	42(27.8)	14(9.3)	23(15.3)
Unknown	151(6.6)	103(68.2)	122(81.4)	116(77.4)
Functional status				
Working	79 (52.3)	129 (85.4)	145(96.7)	143 (95.3)
Ambulatory	68(45.0)	1(0.1)	0(0)	0(0)
Unknown	4(2.6)	21(13.9)	5(3.3)	7(4.7)
Adherence				
Good	148 (98)	140 (91.6)	98 (65.3)	117(78.0)
Fair or Poor	3(0.2)	11(7.4)	52(34.7)	33 (22.0)

DISCUSSION

This study reported that 18 adolescents living with HIV were lost to follow-up after one year of transfer to adult care from a cohort of 151 (11.9%). Although the expectation from adult clinics receiving these adolescents was assuming responsibility for their care tasks, the result of this study showed that they were not prepared for it at the time of transition. This was shown by an increasing proportion of adolescents with poor adherence, reflected by a drop in their CD4 counts, which raised concern in their post-transition care.

The lost follow-up in this study was consistent with findings from Quebec, Canada (10), Atlanta, Georgia (11) and the Netherlands (17). This lost to follow-up could be due to lack of preparation for the transfer and/or difficulty adapting to the new place and health workers. Adolescents may fear being with adults and/ or may think they lose their confidentiality (18). Different follow-up styles between pediatric and adult follow-up clinics may lead to adaptation problems (10). Another study also identified a lack of communication between adult and pediatric clinics and low developmental readiness barriers for successful transition (19). In addition, the age by itself may pose difficulty in shouldering responsibility for their care and follow-up. It is known that adolescents are different from adults in many aspects and need special attention. Adolescent services are believed to bridge pediatric and adult provision of care by delivering age-appropriate communication and physical environments (20). However, the overburdened adult OPDs in TASH setting may not be suitable to offer special attention and follow-up.

At the time of the transfer, 11(7.4%) of adolescents had fair or poor adherence, and six months and one-year post-transfer, this number has increased to 53 (35.1%), 34 (22.5), respectively. Routine CD4 and viral load are laboratory markers to monitor the success of ART. Viral load monitoring was not done for most adolescents, making it difficult to compare; significantly higher number of adolescents had CD4 count below 200 cells/µl at six months of post-transfer.

With regards to post-transfer mortality, there was one death (0.7%) in a year period, which was comparable to the mortality rate among transitioned adolescents in the United Kingdom, which was 0.9 % (21) but much lower than the mortality rate of transitioned adolescents in Canada, which was 8.8% (9).

Although, the adherence problem was lower than the report from Quebec, Canada (10), it was an issue of concern because it is far lower than the UNAIDS target (90% adherence) (22), and coupled with a decrement of CD4. This could also be due to age-related risk-taking behavioral changes seen in adolescents, like discontinuing medication, requiring age-specific adherence counseling and follow-up.

Limitations

The study clearly showed the challenges associated with transfer of care of adolescents living with HIV from pediatric to adult HIV; however, it has several limitations including the retrospective observational study design, adherence was documented using self-report which is subjected to recall bias, and it was not possible to confidently evaluate the predictors of the adverse outcomes observed.

Conclusions

Although most adolescents remained engaged in their follow-up post-transfer to adult care, there was a significant gap in adherence, and significantly higher number of adolescents had a CD4 count of less than 200 cells/µl and treatment failure six months and one year post-transfer. So we strongly recommend developing a guideline for all health care facilities that give HIV care on preparing and transferring adolescents to adult HIV care. In addition, training adolescents on self-care and medication adherence before the transfer, some period of follow up on both pediatric and adult clinics before the transfer, and maintaining the relationship with the peers in the pediatric side are recommended as possible solutions to ease transfer. Further prospective research is needed on this issue to generate more comprehensive and authoritative evidence.

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Conflict of interests: We declare that we have no competing interests.

Authors' contributions

AG and WA conceived and designed the study. All authors (AG, WAmo, WA) prepared the study proposal, participated in data collection, and have analyzed the data. AG drafted the manuscript. WA actively involved in the data interpretation and critically reviewed the manuscript. All authors (AG, WAmo, WA) have read and approved the final manuscript.

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CASE SERIES

CHIKUNGUNYA AMONG PATIENTS WITH PRE-EXISTING RHEUMATOLOGICAL DISEASES: A CASE SERIES AND REVIEW OF LITERATURE

Muhammad Abdur Rahim, FCPS[1*], Shahana Zaman, FCPS[2], Khwaja Nazim Uddin, FCPS[3]

ABSTRACT

Introduction: *Disease chronicity of chikungunya among patients with pre-existing rheumatological diseases is not well-described in the literature. The aim of the study is to discuss the clinical presentation and disease chronicity of chikungunya in cases with rheumatologic diseases supplemented by literature review.*
Methods: *Patients' clinical and laboratory data were recorded in case record forms. They were followed-up for three months to evaluate disease chronicity.*
Results: *Eight patients (mean age, 40.6 years; male, 6) with different pre-existing rheumatological diseases, complicated by chikungunya virus infection were analyzed. Their clinical presentation included fever (8), joint pain (8), rash (3), pruritus (3) and generalized body ache (4). Two patients (2/8, 25%) entered in chronic phase.*
Conclusion: *In spite of common initial clinical presentation, patients with pre-existing rheumatological diseases had higher frequency of post-chikungunya rheumatism.*
Key words: *chikungunya, post-chikungunya rheumatism, rheumatological diseases.*

INTRODUCTION

Chikungunya is one of the fast-spreading viral infections of global concern including Bangladesh, where it is an emerging infection (1, 2). Acute chikungunya is a self-limiting disease; fever and arthralgia/arthritis are the two most common features. Patients may have acute life-threatening complications like encephalitis and cardiomyopathy but much attention is paid to its protracted rheumatological courses (3, 4). Patient may develop definite rheumatological disease *de novo* after an acute chikungunia virus infection (5) but the outcome of patients with pre-existing rheumatological diseases complicated by chikungunya virus infection is scarce in the literature. A series of autochthonous chikungunya cases occurring among native Bangladeshi patients suffering from different pre-existing rheumatological diseases is presented here.

PATIENTS AND METHODS

This case series included eight patients (having pre-existing rheumatological diseases) with confirmed diagnosis of chikungunya virus infection at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM) General Hospital, Dhaka, Bangladesh from May to November 2017. Chikungunya virus infection was confirmed either by reverse transcriptase polymerase chain reaction (RT-PCR) or by immunoglobin M (IgM) against chikungunya virus.

RT-PCR was done by using Qualitative One-Step Real-Time RT-PCR technology in the ABI 7500 DX instrument with SDS software for chikungunya virus. IgM was detected by immunochromatographic test (ICT) for chikungunya IgM/IgG by using commercially available kits manufactured by SD BIOSENSOR, Republic of Korea. Patients' selected demographic, clinical and laboratory data were recorded in case record forms after getting informed written consent. Patients were followed-up clinically and over phone, as appropriate, for three months since the onset of acute chikungunya virus infection.

RESULTS

Eight patients with mean age of 40.6 years and ranging from 32 – 49 years with different pre-existing rheumatological diagnoses, complicated by chikungunya virus infection were analyzed (Table 1). Six of them were males and two were females. They had been suffering from the underlying disease for a mean of 2.5 (range 1 – 11) years. Patients were on remission during their latest follow-up prior acute chikungunya infection.

Clinical presentation included fever (n = 8), joint pain (n = 8), rash (n = 3), pruritus (n = 3) and generalized body ache (n = 4). One patient with fibromyalgia first presented with joint pain and later developed fever.

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Five (5/8, 62.5%) patients had lymphopaenia, six (6/8, 75%) had high erythrocyte sedimentation rate (mean, 41.9/1-h; range, 18 – 62) and high C-reactive protein (mean, 38 mg/L; range, 6 – 78). Diagnosis was confirmed by RT-PCR for chikungunya (n = 1) and by IgM against chikungunya (n = 7). Dengue was excluded in all patients by negative non-structural protein 1 (NS 1) (done by ICT by using commercially available kits manufactured by Humasis Co. Ltd., Republic of Korea).

Treatment consisted of paracetamol and other medications including disease modifying anti-rheumatic drugs (DMARDs) were continued. One patient with fibromyalgia recovered from her symptoms during the acute phase (within three weeks) but the other patient with fibromyalgia and the patient with ankylosing spondylitis (2/8, 25%) continued with joint pain even after three months (entered in to chronic phase) (Table 1).

Table 1: Chikungunya cases with underlying rheumatological diseases (N = 8)

Case number/ Age/ Sex	Underlying diagnosis/ Duration/ Drug(s) (DMARD)	Clinical features	Important laboratory investigations	Diagnostic test for chikungunya	Subacute phase	Chronic phase
Case 1/ 41 years/ Male	Ankylosing spondylosis/ 11 years/ Salphasalazine	Fever Arthralgia/ Arthritis Body ache Rash	Lymphopaenia ESR = 62 mm in 1st hour CRP = 64 mg/L	IgM	Yes	Yes
Case 2/ 32 years/ Female	Fibromyalgia/ 2 years/ Amitriptylin	Fever Arthralgia/ Arthritis Body ache Rash	ESR = 32 mm in 1st hour CRP = 24 mg/L	RT-PCR	Yes	Yes
Case 3/ 49 years/ Female	Fibromyalgia/ 1 year/ Amitriptyline	Fever Arthralgia/ Arthritis Body ache	ESR = 18 mm in 1st hour CRP = 6 mg/L	IgM	No	No
Case 4/ 48 years/ Male	Gout/ 3 years/ Febuxostat	Fever Arthralgia/ Arthritis	Lymphopaenia ESR = 38 mm in 1st hour CRP = 18 mg/L	IgM	No	No
Case 5/ 41 years/ Male	Gout/ 1 year/ Febuxostat	Fever Arthralgia/ Arthritis	Lymphopaenia ESR = 60 mm in 1st hour CRP = 52 mg/L	IgM	Yes	No
Case 6/ 43 years/ Male	Gout/ 3 years/ Febuxostat	Fever Arthralgia/ Arthritis	Lymphopaenia ESR = 52 mm in 1st hour CRP = 24 mg/L	IgM	Yes	No
Case 7/ 35 years/ Male	Rheumatoid arthritis/ 2 years/ Methotrexate	Fever Arthralgia/ Arthritis Body ache Rash	Lymphopaenia ESR = 53 mm in 1st hour CRP = 78 mg/L	IgM	Yes	No
Case 8/ 36 years/ Male	Systemic lupus erythematosus/ 2 years/ Hydroxy-chloroquine	Fever Arthralgia/ Arthritis	Lymphopaenia ESR = 20 mm in 1st hour CRP = 6 mg/L	IgM	No	No

[DMARD = disease modifying anti-rheumatic drugs, ESR = erythrocyte sedimentation rate, CRP = C-reactive protein, IgM = immunoglobulin M, RT-PCR = reverse transcriptase polymerase chain reaction]

DISCUSSION

Post-chikungunya rheumatisms is an established sequel, though prevalence varies in different countries and regions, may be due to different genetic characteristics, immunological phenomena and the criteria used for detection of post-chikungunya rheumatism (3, 4, 6 -8).

Not only that, the post-chikungunya rheumatism is an established entity, rather evaluation of post-chikungunya rheumatism revealed that an infective episode by chikungunya virus may unmask chronic rheumatism in genetically predisposed individuals; an infective episode may trigger the immunopathogenic reaction necessary for the underlying disease activation (5, 9, 10).

We followed-up our patients for three months with the aim to evaluate whether they enter into chronic phase. One-quarter (25%) of the patients were still experiencing musculoskeletal symptoms, which was much higher than a Bangladeshi chikungunya cohort of 107 cases without any pre-existing rheumatic diseases, where 1 of 11 cases (9.1%) had entered into chronic phase (11). Unfortunately, we failed to find any information in the literature, regarding post-chikungunya chronic rheumatism among patients with pre-existing rheumatological diseases and this observation prompted us to report the present series.

Patients with post-chikungunya rheumatism were managed differently and there is a published guideline for such management by the Brazilian Society of Rheumatology (12). Outcome of musculoskeletal symptoms of chikungunya infection among patients with and without pre-existing rheumatological diseases are lacking in the literature. We predict that patients with underlying rheumatological diseases behave differently and a longer follow-up of larger cohorts will answer this question adequately.

Conclusion

We concluded from the findings of this case series that, patients with pre-existing rheumatological diseases, when infected by chikungunya virus, may have similar clinical presentation of those without prior such diseases but have a higher chance of suffering from post-chikungunya rheumatism. We propose to follow-up the chikungunya cases, especially for rheumatological courses and we emphasize patients with pre-existing rheumatological diseases merit special attention in this regard.

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Conflict of interest: Nothing to declare.

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Daniel Hailu, Dagnachew Tamirat, Amezene Tadesse, Daniel Zewdneh Solomon. *Ethiop Med J, 2021, Vol. 59, No. 3*

CASE REPORT

RHABDOID TUMOR OF THE KIDNEY IN A FIVE MONTHS OLD FEMALE INFANT

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ABSTRACT

Rhabdoid tumor of the kidney is a very rare disease with poor overall survival. We report a five- month- old female infant who was diagnosed to have Stage IV Rhabdoid Tumor of the kidney at a tertiary institution in Ethiopia. She presented with hematuria of 1 week duration and on physical examination had a 6 x 8 cm right bimanually palpable abdominal mass. She had stage II hypertension. She had persistent hypercalcemia which resolved in the post-operative period. A left radical nephrectomy and para-aortic lymph node excision were done. The diagnosis was biopsy proven and supported by imaging. The infant was put on ifosfamide, carboplatin and etoposide but died 12 days after onset of the first cycle from sepsis. Rhabdoid tumor of the kidney is very rarely reported from low-income countries. Awareness of this disease may help in early detection and better prognosis.

***Keywords**: Rhabdoid Kidney. Hypercalcemia. Hypertension. Hematuria .Ethiopia*

INTRODUCTION

Rhabdoid tumors of the kidney (RTK) are one of the most lethal and aggressive diseases with a poor outcome. Rhabdoid tumor of the kidney was first reported as a distinct histopathologic entity in 1978 (1). It was described as a "rhabdomyosarcomatoid pattern".

This rare but aggressive malignancy accounts for 2% of paediatric renal tumours with 80% occurring in those under the age of 2 years and 60% in those under the age of 1 year, and has an overall male predominance (ratio 1·5:1) (2). RTK accounts for an estimated 0.9 -2 % of renal cancers (3, 4). The age ranges from 3 weeks to 94 months.

The median age was 7 months (3). Tumors of higher stage and younger infants were associated with an overall survival of 15.9% and 8.8%, respectively (5).
We report a five months old female infant who was diagnosed to have stage IV RTK and hypercalcemia at the largest tertiary hospital in Ethiopia, Tikur Ambessa Specialized Hospital (TASH).

Case presentation

A five months old female child from Adama City (99 kilometers outside Addis Ababa) presented with an initial complaint of recurrent reddish discoloration of urine of 1week duration.

The infant had no fever, vomiting or crying on micturition. She was diagnosed as having urinary tract infection at a local clinic and started on an unspecified antibiotic which she took for 4 days. She underwent an abdominal ultrasound scan since her symptoms had persisted. The study revealed a left renal mass and she was then referred to TASH.

The parents had not noticed any abdominal enlargement or palpable swelling earlier. The pregnancy was uneventful. Prenatal care ultrasound examinations done during antenatal care were non-revealing. The infant was born at term and had no events following delivery. The infant had no history suggestive of any bleeding disorders. Apart for the unspecified antibiotic, she had not been on any other drugs.

She was exclusively breast fed and vaccinated for her age according to the adopted national schedule. She was able to support her head at 3 months of age. She had started to sit up supported. She was the second child of two. Her parents and her elder sister were apparently healthy.

Her examination revealed a comfortable infant breast feeding quietly. The infant had no dysmorphic features. Apart for her BP, her other vital signs were within the normal range. Her blood pressure was in the range of 100 -118/ 85- 90 (Stage II hypertension).

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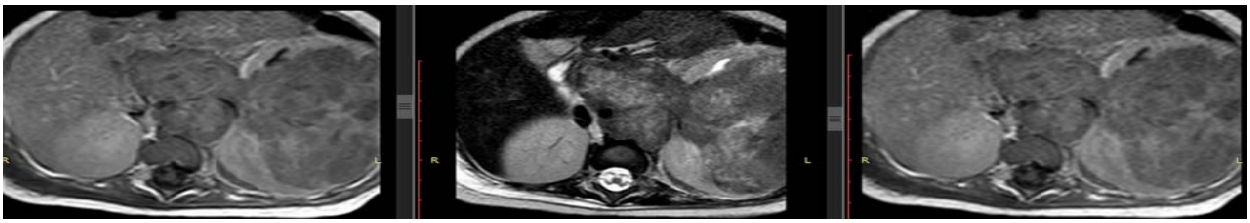
Her anthropometry was not affected. She had pink conjunctivas and non-icteric sclera. No palpable lymph nodes or glands. The pertinent physical finding was a 6 x 8 cm bimanually palpable non-tender firm lumbar right mass. In addition to these findings the infant had palmar pallor. The external female genitalia were normal. The infant was alert with a normal neurological examination. There were no abnormalities in other systems.

Prior to surgery, the laboratory studies revealed serum calcium in the range of 2.63 -5.88 mmol/L (normal range 1.1 – 1.25). Post- surgery serum calcium dropped to 1.23 mmol/L. The urine analysis revealed microscopic hematuria of 10 -12 RBC/mm3. CSF analysis was normal without any cells. The CSF cytology showed no malignant cells.

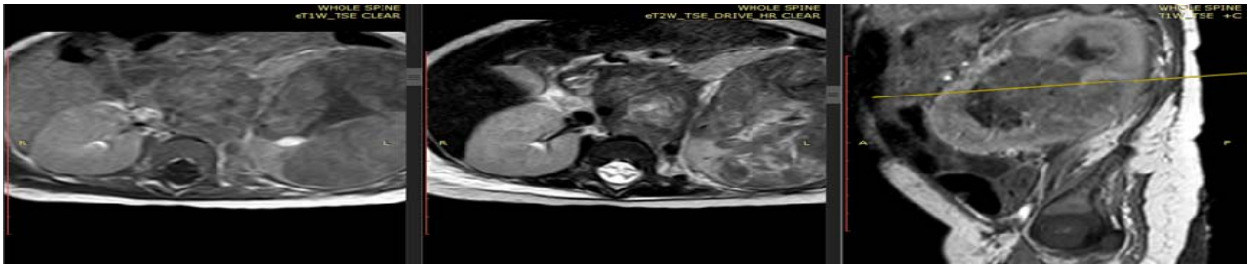
The infant was on anti-hypertensives (oral nifedipine, oral atenolol and repeated intravenous doses of hydralazine) medication for stage II hypertension. She showed no response to treatment. Following the surgery, the hypertension resolved and the medications were stopped.

The infant was started on ICE (Ifosfamide, carboplatin and etoposide) protocol. The infant developed febrile neutropenia post – chemotherapy. Her absolute neutrophil counts were below 500 / mm3 with temperature records of 38.5° C and above. Despite potent intravenous antibiotic coverage, she died within 72 hours of sepsis on day 12 post – ICE. Blood culture revealed no growth.

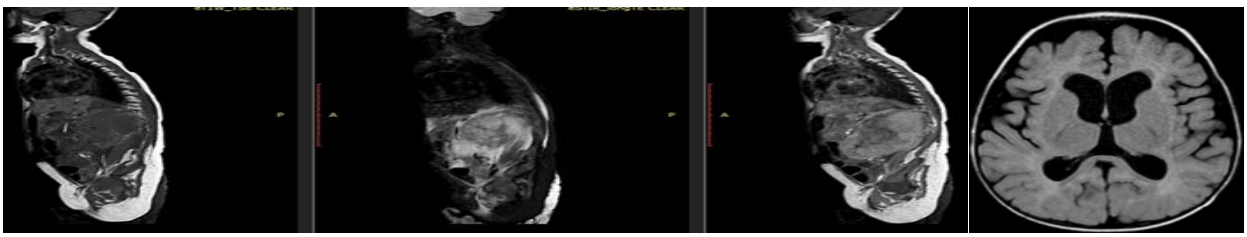
A Radiology report



A T1 axial T2 axial T1 + C sagittal



B T1 axial T2 axial T1 + C sagittal



C T1 sagittal T2 sagittal T1 sagittal PC FLAIR

D : Chest CT scan

Figure 1: there is a huge heterogenous mass lesion with solid and cystic components in the left kidney with heterogenous enhancement forcing a moderate pelvi-calyceal dilatation. There are multiple sites of low signal intensities indicating tumor lobules. There are also associated left para-aortic huge lymph nodes elevating the aorta **(A&B)**. There are multiple lung nodules visible in the basal lung fields **D**. There was no brain or spinal lesions seen **C (PC: post contrast)**

Intra-operative findings

A left renal mass measuring approximately 8 x 7 cm in size was found. There was a huge para-aortic lymph node in the hilar area extending anteriorly which was closely adherent to the aorta.

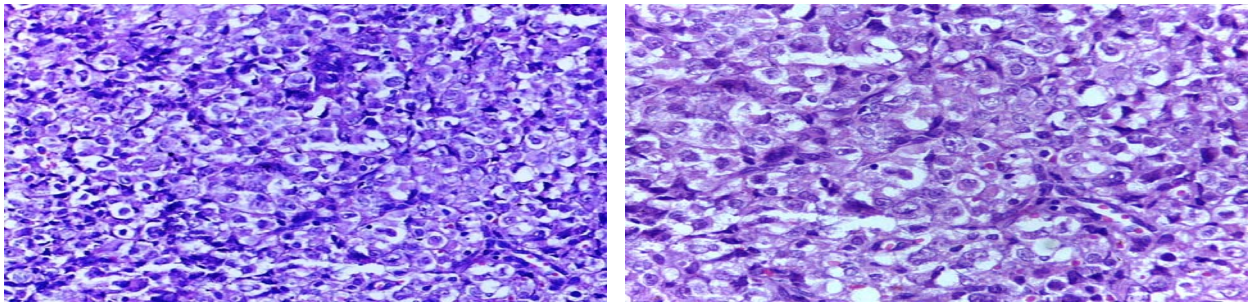
A left renal radical nephrectomy was done. Two lymph nodes were sampled. Since lymph nodes were in close proximity to the aorta, further sampling was not possible.

Pathology

Gross specimen examination revealed gray brown capsulated nephrectomy specimen measuring 8x6.5x6 cm. Cut-section showed grey-brown tumor mass measuring 7.5x 5x6cm filling most of the cortex and renal medulla with capsular invasion at two points. Non-neoplastic renal tissue measuring 0.5x1 cm and 0.5X0.5cm at each pole was present. About 40% was necrotic in the tumor mass.

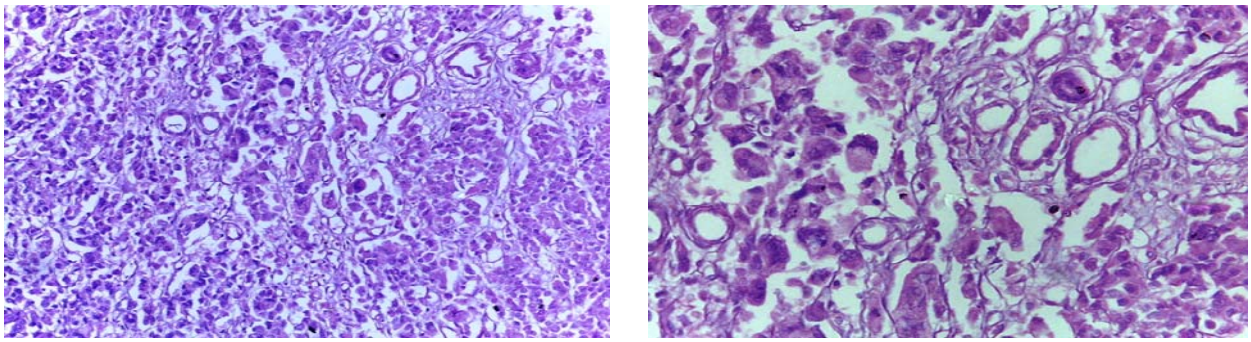
Two gray white para-aortic lymph nodes measured 0.8cm and 0.6cm in greatest dimension.

On histopathological examination, round to oval tumor cells were seen arranged in sheets, having pleomorphic vesicular nuclei and prominent nucleoli (Figure 2A and 2B). These tumor cells showed moderate to abundant amount of eosinophilic cytoplasm and hyaline intracytoplasmic inclusions (Figure 3A and 3B). There was increased mitotic activity with large areas of necrosis. Few sections showed renal tissue with glomeruli and tubules. Histologic sections from the para-aortic lymph nodes showed secondary infiltration by similar tumor cells**.**



A **B**

Figure 2: Rhabdoid tumor of the kidney: (A) round to oval tumor cells arranged in sheets, having pleomorphic vesicular nuclei and prominent nucleoli (hematoxylin & eosin, 200×), (B) High power microscopic findings of tumor cells with acidophilic cytoplasm (hematoxylin & eosin, 400×)



A **B**

Figure 3: (A) Large cells with eccentrically located nuclei and abundant, eosinophilic cytoplasm overrunning tubules (hematoxylin and eosin, 200×), (B) High power microscopic of similar tumor cells (hematoxylin & eosin, 400×).

DISCUSSION

The diagnosis of rhabdoid tumor of the kidney (RTK) was made based on the characteristic findings of vesicular chromatin, prominent nucleoli and hyaline cytoplasmic inclusions. With lung involvement, the infant was staged as stage IV at presentation (advanced disease). Tomlinson et al study showed most infants had advanced disease at presentation (5). In their publication, lung metastasis accounted for 28.9%. Most had multiple lesions in both lung fields and were unresectable as depicted in our report.

The inconsistent availability of proper diagnostics in low income countries makes it challenging to do immunohistochemistry and genetic testing. The RTK immunohistochemistry would be positive for vimentin, EMA and negative for INI1 (8). In addition, RTK and extra-renal rhabdoid tumors all share a SMARCB1 mutation at chromosome 22q11-12 (8, 9). This could be germline or somatic mutation .The median age group for germline mutations was 6 months of age (9). Considering our client's age, germline mutation is a possibility.

Symptoms, signs and laboratory evidence related to RTK include hematuria, hypertension, and hypercalcemia. Amar et al study showed that hematuria (gross/ microscopic) and hypercalcemia were present in 84% (22/37) and 26 %(6/23) of cases, respectively (10). Mary M et al study, hypercalcemia, hypertension and hematuria were present in 19%, 11% and 43 % respectively (11). The presence of hematuria, hypercalcemia and hypertension could be considered as supportive evidence for the disease in our case.

The characteristic radiologic evidence for RTK reported above (6, 7) and consistent intra-operative findings of extensive disease are supportive of the diagnosis.

The prognosis of young infants with advanced disease treated on conventional chemotherapy, in high income countries, has been dismal (5). Though our client died as a consequence of toxicity, she would have had a similar fate if she had survived.

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Conflict of Interest :
We have no conflict of interest to reveal.

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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 resubmitting 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.

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THE ETHIOPIAN MEDICAL JOURNAL

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