#### **ORIGINAL ARTICLE**

# ADNEXAL TORSION A FIVE-YEARS RETROSPECTIVE REVIEW IN TWO HOSPITALS

Zeleke Sahlu, MD<sup>1</sup>, Shiferaw Negash, MD<sup>1</sup>, Lukman Yusuf, MD, PhD<sup>1</sup>

#### **ABSTRACT**

**Background:** Adnexal torsion remains a challenging diagnosis, often leading to delayed operative intervention and resultant ovarian loss.

**Objective**: To describe the clinical profile and therapeutic approaches of adnexal torsion in the Ethiopian setting. **Methods:** A retrospective cross sectional descriptive chart review of women with surgically proven adnexal torsion was conducted in two teaching hospitals from Jan1 2007- Dec 31, 2011.

**Results:** A total of 53 women with AT were analyzed. About 33(62%) of torsion occurred in the age group of 20-29 years. The most common symptoms were lower abdominal pain 52 (98.1%) followed by nausea and vomiting 46 (86.8%), whereas, the common physical findings were lower abdominal tenderness 49(92.5%) and palpable pelvic mass 40 (76.9%). Adnexal torsion was considered in the differential diagnosis upon initial evaluation only in 27 (51%) of the cases.

Of the study subjects, only 7(13.2%) had surgery within 24 hours of arrival to the facility and the mean time from initial evaluation to surgery was  $53.8\pm44.5$  hours. Moderately positive correlation was observed between ultrasound and intra-operative adnexal size measurement (r = 0.716, p = 0.000).

Using non-parametric independent sample test, none of the clinical profile categories studied show significant difference in mean time from initial evaluation to surgery. Despite the overwhelmingly benign pathology, most 46 (86.8%) of patients underwent adnexectomy with only 3(5.7%) adnexal salvage rate.

**Conclusion:** Delayed surgical intervention and low ovarian salvage rate inspite of predominantly benign pathology was observed. Therefore, high degree of suspicion, especially in patients with high risk factors, and timely intervention must be exercised in an effort to salvage the adnexae.

Keywords: Adnexal, Torsion

# **INTRODUCTION**

Adnexal torsion (AT) is the fifth most common gynecologic emergency and affects females of all ages and accounts for 2.7% of surgical emergencies and 15% of surgically treated adnexal masses (1,2). Adnexal torsion is a well-known yet poorly recognized clinical entity that can involve the rotation of the tube, ovary, and ligaments either separately or together, leading to obstruction to blood flow, with subsequent ischemic necrosis of the torsed structures, unless timely intervened, results in loss of these tissues (3). Mostly, the ovary and fallopian tube rotate as a single entity around the broad ligament. Infre-

quently, the ovary and rarely the fallopian tube may twist alone around their mesentery (4).

Adnexal torsion can occur at any age, but mostly occurs in the early reproductive years. The median age reported by a large review was 28 years, with the percentage of patients younger than 30 years is approximately 70-75%. Functional cysts and benign neoplasm accounted for 94% of the cases, with the remainder occurring in the setting of normal appearing ovaries (5). Adnexal torsion has been attributed to a variety of etiologies. Certain causes are more likely in particular age groups; while anatomic factors usually account for AT in adults, normal ovaries have been demonstrated in over 50 percent of AT in children under the age of 15 years (1).

<sup>&</sup>lt;sup>1</sup>Department of Obstetrics and Gynecology, Collage of Health Sciences Addis Ababa University

Though, confident and early diagnosis of adnexal torsion is imperative, failure to consider it in the differential diagnosis is not uncommon, given the relative infrequency of this condition. Consideration is particularly crucial in a patient with known risk factors for the disease, such as ovarian mass, prior pelvic surgery, or pregnancy (6).

The diagnosis of AT can be challenging, because the symptoms are relatively non-specific. A definitive diagnosis of adnexal torsion is based upon surgical findings. The clinical diagnosis should be considered in girls or women with lower abdominal pain, especially in the setting of ovarian cyst/mass, and is primarily a clinical judgment that utilizes imaging modalities as adjuncts to complete the clinical picture (1, 7-10). In a review of fifty-nine patients with AT, the two most common presenting features were lower abdominal pain and adnexal mass, 83% and 72%) respectively (10).

Delayed presentation of women resulting in loss of the adnexa due to irreversible damage was shown in a retrospective chart review among 87 surgically confirmed adnexal torsion cases, where, detorsion and salvage was possible only in 8 (9%) patients, and 26 (29.2%) patients had surgery within 24 hours (6). Ovarian salvage rate of 0% to 7 % reported by other studies (7, 8). Therefore, the mainstay of treatment is swift operative evaluation to preserve ovarian function and prevent infectious complications. Historically, removal of the affected adnexa had been the standard treatment of the torsed adnexa, because, it was believed that restoring normal anatomy via detorsion could dislodge a clot in the ovarian vein and subsequent embolism, or leave a necrotic vestige. Despite this pervading theory, there is growing evidence that unwinding the involved adnexa to observe for tissue reperfusion and viability is safe, and currently the minimally invasive surgical management of adnexal torsion has been increasing in efficacy (5,11-16).

Multiple reports over the past 15 years have described minimally invasive procedures that detorsed and preserved the ovary without the hypothesized adverse sequelae and with return of normal hormonal function and fertility. These and other data suggest that detorsion and ovarian preservation is a safe operation that should be considered in premenopausal patients (6, 17-25). In addition, histopathology of the torsed adnexa was reported to be benign in over 90%, and hence, benign neoplasms are more likely to undergo torsion than malignant ovarian neoplasms (16, 17).

In a retrospective review of all women less than 40 years old with adnexal torsion, all potentially viable adnexa were untwisted, and cystectomies were performed unless the adnexa failed to reperfuse. Of the ninety-four women studied, 61(65%) received ovarian cystectomies and 33(35%) underwent salpingooophorectomy. No thromboembolic complications or increase in post-operative morbidity was seen. Patients requiring salpingo-oophorectomy had more pre -operative fever and leukocytosis, larger masses, and higher degrees of torsion (26). Therefore, the paradigm has now shifted from one of ovarian removal to one of ovarian evaluation and likely preservation, even in the face of a dusky, seemingly necrotic appearance. However, the diagnostic dilemmas and difficulties in preserving the ovaries in lately appearing women is still of major concern(1).

There is no study so far conducted in Ethiopia regarding adnexal torsion. The objective of this study is therefore, to describe the demographic characteristics, clinical profile, imaging and laboratory findings, possible causes, diagnostic challenges, and mode of management in women with surgically proven AT.

#### MATERIALS AND METHODS

A cross sectional retrospective descriptive study was conducted in the two hospitals, Tikur Anbassa Hospital and Saint Paul's Hospital, which are specialized referral and teaching hospitals in Addis Ababa, used by the Department of Obstetrics and Gynecology, College of Health Sciences, Addis Ababa University, for both undergraduate and postgraduate training programmes. These hospitals serve as the main referral centres in the city and its vicinity, with 24 hours multi-disciplinary specialty care, provided by residents with specialist supervision, for all gynecologic and surgical emergencies. In addition, the two hospitals carry out about 1200 major gynecologic surgeries per year, have an intensive care units and blood transfusion facilities, with experienced consultants in the field of Obstetrics and Gynecology as well as Anesthesiology. Gandhi Memorial Hospital (GMH), a maternity referral hospital under the Addis Ababa City Administration Health Bureau, was excluded from the study, as women presenting with acute abdomen accompanied with diagnostic dilemmas were referred to the aforementioned hospitals. In addition, as a preliminary assessment, review of GMH major operation registry book was done and only one surgically confirmed case was found over the five years study period.

The study design was a five years retrospective chart review, conducted from Jan1, 2007 – Dec 31, 2011, involving all women who visited the study sites during the study period, with surgically confirmed cases of AT, or women for whom AT was considered as a differential diagnosis on initial examination if evaluation note is accompanied by time, initial laboratory or imaging requests or anything on the card suggesting its precedence over the other evaluation. Subjects were excluded if AT was not confirmed surgically or torsion of paratubal or paraovarian cyst or mass was not involving the ovaries.

Using structured checklist prepared in English, data was collected by trained Obstetric and Gynecology residents on the variables of interest. The major operation theatre registries of the hospitals were used to retrieve card numbers of the study subjects, and then patients' cards were collected from the card rooms of the respective hospitals. Data was checked for completeness, consistency, and accuracy, then, analyzed using SPSS version 20 statistical software. Frequency distribution tables, mean, and median were used where appropriate to describe quantitative variables, whereas charts and proportions were used to describe qualitative variables. Non-parametric Independent Samples T-test and Bivariate correlations were used to measure associations, with 95% confidence level and level of significance set at  $\alpha = 5\%$ .

Ethical clearance was obtained from research and publication committee of the Department of Obstetrics and Gynecology, College of Health Sciences, Addis Ababa University. Permission to conduct the study in the chosen hospitals was secured from responsible bodies. Information in the charts were used solely for the current research purposes, and names of patients' or card number were not described in the study.

# **RESULTS**

Over a period of 5 years, a total of 73 charts were identified from major operation registry books, 48 from Saint Paul's and 25 from Tikur Anbessa Hospitals. Of these, 53 cards with surgically confirmed adnexal torsions were retrieved, 38 (71.7%) from SPH and 15 (28.3%) from TAH. Torsed paraovarian/paratubal cysts or masses in which the ovary was uninvolved (n = 3) were excluded so as not to improve ovarian salvage rates falsely; the rest, 17 charts could not be located.

The age distribution ranges from 17-75 years with median of 26 years. Thirty three (62%) of the AT occur in the age group of 20-29 years, and 38 (73.6%) of AT occur in the age groups of 29 years and below. Majority 36 (68%) are from Addis, 20 (37.7%) are married, and 16 (30.2%) being single (Table 1).

The patients' symptom characteristics were variable. Lower abdominal pain was manifested in 52 (98.1%) and nausea and vomiting accounted for 46 (86.8%) of patients with AT. History of previous surgeries, cesarean sections, were reported only in 2 (8%) of the subjects.

Among 34 patients who had their temperature recorded, only 8 (23.5%) had objective record of fever. Lower abdominal tenderness and palpable pelvic mass were reported in 49 (92.5%) and 40 (76.9%) of patients, respectively. Adnexal torsion was considered in the differential diagnosis upon initial evaluation only in 17 (32.1%) patients, the rest being either not reported or documented (Table 2). The statistical association of pelvic pain, nausea and vomiting, fever, lower abdominal tenderness, and palpable adnexal mass, were compared with the presence of adnexal torsion in the initial differential diagnosis, but due to small observations, no valid result could be generated.

Table 1. Socio-demographic characteristics of women with adnexal torsion, TASH and SPH, Jan 1, 2007-Dec 31, 2011

| Characteristics    | Value                  | Number (N=53) | Percent |
|--------------------|------------------------|---------------|---------|
| Address            | Addis Ababa            | 36            | 67.9    |
|                    | Out of Addis           | 17            | 32.1    |
| Age                | 15-19                  | 6             | 11.3    |
| 8                  | 20-24                  | 14            | 26.4    |
|                    | 25-29                  | 19            | 35.9    |
|                    | 30-34                  | 4             | 7.5     |
|                    | ≥35                    | 10            | 18.9    |
| Occupation         | Housewife              | 12            | 22.7    |
| •                  | Student                | 5             | 9.4     |
|                    | Gov't / self-employees | 8             | 15.1    |
|                    | Not documented         | 28            | 52.8    |
| Marital Status     | Single                 | 16            | 30.2    |
| 1.2002 2000 200000 | Married                | 20            | 37.7    |
|                    | Divorced /widowed      | 6             | 11.3    |
|                    | Not documented         | 11            | 208     |

<sup>\*</sup> Government employees, self employees and daily laborer \*\* Divorced and widowed

Table 2 – Clinical Presentation of Patients with Adnexal Torsion, TASH and SPH, January 1, 2007- December 31, 2011.

| Symptoms and Signs        |                | Frequency $(n = 53)$ | Percent |
|---------------------------|----------------|----------------------|---------|
| Pelvic pain               | Yes            | 52                   | 98.1    |
|                           | No             | 1                    | 1.9     |
| Nausea and vomiting       | Yes            | 46                   | 86.8    |
| _                         | No             | 7                    | 13.2    |
| Pelvic surgery            | Yes            | 2                    | 3.8     |
|                           | No             | 51                   | 96.2    |
| Fever                     | Febrile        | 8                    | 15.1    |
|                           | Afebrile       | 26                   | 49.1    |
|                           | Not documented | 19                   | 35.8    |
| Adnexal tenderness        | Yes            | 49                   | 92.5    |
|                           | No             | 4                    | 7.5     |
| Palpable Adnexal Mass     | Yes            | 40                   | 75.5    |
| 1                         | No             | 12                   | 22.6    |
|                           | Not documented | 1                    | 1.9     |
| Adnexal torsion Diagnosis | Yes            | 17                   | 32.1    |
| _                         | No             | 16                   | 30.2    |
|                           | Not documented | 20                   | 37.7    |

Of the study subjects, 13 (24.5%) were pregnant, with gestational age that ranges from 6-27 weeks, of which, 10 (77%) were first trimester pregnancies. Of the 48 (90.6%) study subjects, who had ultrasound examination, 44(91.6%) had abnormal results (cyst, solid or complex mass), and in 4 (8.6%) patients' ultrasound results was non-revealing. The size of the mass measured by the ultrasound ranges from 5-20 cm with the mean of 8.5±3.2 cm, and 27 (59.1%) of AT had a mass with a size between 6-8 cm (Fig. 1). Doppler study together with ultrasound was done only in 3 (6.3%), of which, only one showed compromised vascular flow (absent vascular flow). Despite this, most appeared gangrenous on laparotomy, and, adnexectomy was performed.

The time interval from the onset of symptoms to arrival for evaluation by health professional ranged from 4-96 hours, with the mean of  $21.6 \pm 19.2$  hours. Only 14(26.4%) patients with AT arrived within 24 hours, and 7 (13.2%) patients had surgery within 24 hours after arrival to the facility. The mean time from initial evaluation to surgery was  $53.8 \pm 44.5$  hours (range = 4 to 168 hours), and similarly, duration of time spent from onset of symptom to surgery (range= 10 - 192 hours), mean,  $74.7 \pm 46.3$  hours.

Non-parametric Independent Samples (Mann Whitney U) test was used to check if presence or absence of clinical manifestations, pregnancy test, and ultrasound result were different in mean time from initial evaluation to surgery. However, none of clinical profile categories had statistically significant difference in mean time from their counterparts. Pelvic pain (p = 0.067), nausea and vomiting (p = 0.883), fever (p = 0.401), adnexal tenderness (p = 0.647), diagnosis of adnexal torsion on initial evaluation (p = 0.058), pregnancy test (p = 0.691), ultrasound result (p = 0.621).

When intra-operative finding were considered, majority, 31 (58.5%) occurred on the right side and the rest occurred on the left, and, almost all, 52 (98.1%) appeared gangrenous, the remaining one was not documented. The median degree of adnexal torsion was 720. In this study due to the low salvage rate, association couldn't be computed. Regarding consistency of the adnexae, 38 (71.7%) were cystic followed by 10 (18.9%) solid. The intra-operative mass size ranges from 4-24 cm, with the mean of  $10.8\pm4.3$  cm (Table 3).

Table 3 - Intraoperative Findings and operative procedures of Patients with Adnexal Torsion, TASH and SPH, January 1, 2007-December 31, 2011.

| Intraoperative Findings |                                | Frequency $(n = 53)$ | Percent |
|-------------------------|--------------------------------|----------------------|---------|
| Side of adnexal torsion | Right                          | 31                   | 58.5    |
| occurred                | Left                           | 22                   | 41.5    |
| Consistency of torsed   | Cystic                         | 38                   | 71.7    |
| adnexa                  | Solid                          | 10                   | 18.9    |
|                         | Complex                        | 5                    | 9.4     |
| Appearance of torsed    | Gangrenous                     | 52                   | 98.1    |
| adnexa                  | Not documented                 | 1                    | 1.9     |
| Attempt of detorsion    | Yes                            | 8                    | 15.1    |
|                         | No                             | 45                   | 84.9    |
| Adnexal salvage         | Yes                            | 3                    | 5.7     |
| -                       | No                             | 50                   | 94.3    |
| Type of procedure done  | Adnexal salvage with resection |                      |         |
| · ·                     | of tumorous mass               | 3                    | 5.7     |
|                         | Oophorectomy                   | 3                    | 5.7     |
|                         | Salpingectomy                  | 1                    | 1.9     |
|                         | Adnexectomy                    | 46                   | 86.8    |

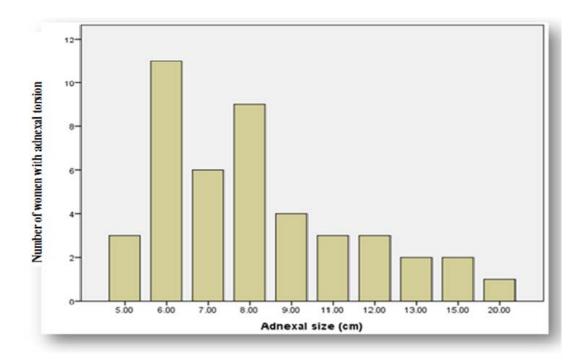


Figure 1 - Size of Torsed Adnexae Measured by Ultrasound, TASH and SPH, January 1, 2007- December 31, 2011.

The mean adnexal size was  $10.8 \pm 4.3$  cm versus  $8.86 \pm 3.29$  cm in the intra-operatively estimated and transabdominal measurement, respectively. Using Nonparametric Spearman's correlation, the preoperative ultrasound and intra-operative adnexal size measurements show moderate positive correlation, r = 0.716, p < 0.000 (Figure 2).

Adnexectomy was the commonest procedure 46 (86.8%) performed for the patients. Detorsion was performed in 8 (15.1%) patients, and, only 3(5.7%) of these patients had resection of an accompanying cyst or complex neoplasm with salvage of the adnexa (Table 3).

From 39 (73.6%) pahology results available, the resultant histologic types were:functional cysts, 18 (46.2%), necrotic or edematous ovarian tissue with no identifiable underlying pathology and benign neoplasms each contributing to 10 (25.6%), and only 1(2.6%) reported to be malignant (serous cystadenocarcinoma) (Table 4).

There was no immediate complications encountered following detorsion or adnexal salvage, though, subsequent ovarian viability in these patients was not assertained.

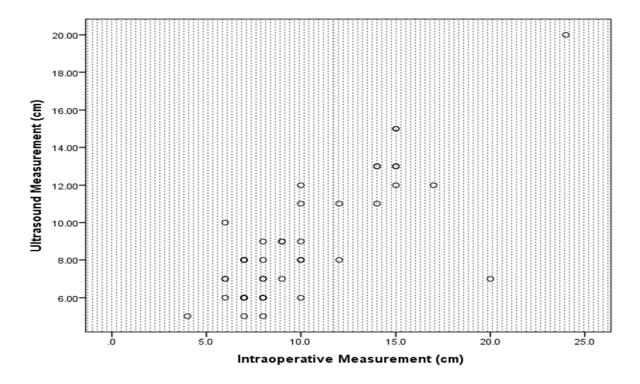


Figure 2 - Scatter Diagram Showing Moderate Positive Correlation of Preoperative Ultrasound and Intraoperative Adnexal Mass Measurements, TASH and SPH, January1, 2007-December 31, 2011.

Table 4 – Pathologic Classification of Torsed Adnexae, TASH and SPH, January 1, 2007- December 31, 2011.

| Pathology result                                | Frequency $(n = 53)$ | Percent |
|---|----------------------|---------|
| Necrotic/infracted tissues                      | 10                   | 18.9    |
| Cystic (functional)                             | 18                   | 34.0    |
| Serous cystadenomas                             | 6                    | 11.3    |
| Mucinuouscystadenomas                           | 1                    | 1.9     |
| Dermoid cyst                                    | 2                    | 3.8     |
| Benign Brenner tumor                            | 1                    | 1.9     |
| Serous cystadenocarcinoma                       | 1                    | 1.9     |
| Not documented (pathology result not available) | 14                   | 26.4    |

#### **DISCUSSION**

Adnexal tortion was considered in the initial differential diagnosis in nearly a third of the cases in our study. Thus, it appears from many studies, including ours, the majority of patients with AT have a delayed diagnosis due to the non-specific nature of the clinical presentations (1, 7-9).

Similar to other reports, our study revealed that about 62% of adnexal torsion occurrence in the age group of 20-29 years. This best describes the teaching that age is a strong corollary for hormonal development, which can influence the incidence of torsion caused by ovarian cysts. Reproductive age women were shown to have the highest incidence of ovarian torsion. This is likely to be related to the higher frequency of physiological and pathological ovarian neoplasms, infertility therapy, and pregnancy in this age group compared to younger or older females (5, 15).

The commonest clinical presentations observed in our patients; lower abdominal pain, nausea and vomiting, lower abdominal tenderness, and palpable pelvic mass were similar to other studies (10). Objective findings were also variable and rarely impressive in patients with AT. In fact, this paucity of objective findings may be a clue that AT should be considered. Although ovarian necrosis can cause leukocytosis and fever; laboratory abnormalities were non-diagnostic and WBC count were unremarkable in the majority of patients in our study, as was temperature derangement.

As physical examination findings are often non-specific, imaging studies are frequently used in the evaluation of a patient with lower abdominal pain. Ultrasound is the imaging modality of choice for adnexal torsion, as it is non-invasive and avoids radiation exposure. In this study, ultrasound detected 91.7% of enlarged adnexa associated with AT. Admittedly, in our study, all ultrasound studies were done via a transabdominal approach, although, obesity or extreme abdominal tenderness can limit the study and may have impacted the sensitivities. But the sensitivity of doppler flow studies of the ovaries has yet to be determined. Any flow found in the

ovary by duplex can delay operative intervention. Although doppler flow imaging with morphologic assessment (e.g., ovarian masses) has been reported to improve the accuracy of diagnosing AT, our study found out that doppler flow still missed 2 of the 3 patients with AT (5, 8).

Ther observed preferential sidedness of torsion to the right in our study is in agreement with the expected 3 to 2 ratio (right to left) and has been attributed to the relative mobility of the cecum allowing for more ovarian movement, in comparison to the relative fixation of the sigmoid colon (8). Contrary to the current recommendation of detortion of all potentially viable ovaries and subsequent ovarian salvage rate of 9-65% by various investigators, our study demonstrated only 15% detortion and 5.7% ovarian salvage rate (4, 18, 25).

Among patients whose adnexae were salvaged, only one underwent surgery within 24 hours after the onset of symptoms, the rest were done 2.5 to 5 days later. Only 2 (3.8%) patients had surgery within 24 hours of arrival to the hospital. This can be explained with both the patients' and the health care providers' delay; for the patients, the onset of symptom may assume milder form not urging to seek health care, and for the health care provider, it is obviously due to the associated diagnostic confusion. Another study revealed a significant association between waiting periods for surgery more than 10 hours and diagnosis of adnexal necrosis. The contemporary philosophy for salvaging the ovary when at all possible, stems from concerns of decreased fertility as a result of the loss of even a single ovary because of decreased ovarian reserve and a reduced reproductive life span. The low ovarian salvage rate observed in our study limits our ability to find statistical correlation between salvage and other metrics (clinical presentation, imaging, and laboratory study time to surgery) (6, 17-24).

Malignancy as a source of the enlargement in most series is rare. This was supported by our finding, where, 97.4% of the pathology were simple cyst or benign tumors. Similar result was reported from a review of histopathology of the torsed adnexa, where, over 90% were benign, and hence benign neoplasms are more likely to undergo torsion than malignant ovarian neoplasms (16, 17). There is so far no laparoscopic approach was made both for diagnosis and treatment in this study, despite the fact that it is of paramount importance in salvaging the adnexa and clearing the diagnostic confusion (16-18).

Conclusion and recommendations: Ovarian torsion remains a diagnostic dilemma and a diagnosis of exclusion. This study demonstrated strong association of torsion with a pelvic mass larger than 5 cm measured by ultrasound in 92% of cases. Therefore, with coexistence of one or more clinical profiles (pain, nausea and vomiting, abdominal tenderness and pregnancy), it is prudent to consider diagnosis of adnexal torsion and expedite surgical management in an effort to preserve ovarian function and prevent adverse sequelae (necrosis, infarction, local hemorrhage, peritonitis, and systemic infection). A 2% risk of malignancy in the torsed ovaries combined with the commonly affected age being young, supports the implementation of detorsion at initial operation.

As this study is the first of its kind, its contribution towards the knowledge of AT in the country can not be undermined. However, the study population can neither be representative of the population of the city nor the country, as these hospitals manage more complicated cases. Some data retrieved from the cards were incomplete because of the nature of the study design (retrospective), we therefore, recommend a prospective large scale study in the future. We further recommend the use of minimally invasive surgical technique, for women presenting with acute abdominal pain and a pelvic mass which might help shorten the prolonged presentation to surgery time and help salvage the adnexae.

#### **ACKNOWLEDGEMENTS**

We would also like to thank the Research and Publication Committee of Obstetrics and Gynecology, College of Health Sciences, AAU, for approval and readiness for provision of ethical clearance. Furthermore, we acknowledgethe hospital directors of the study sites for having accepted the ethical clearance letter and allowing us to undertake the study.

We extend our heartfelt gratitude to Tsion Sahle, secretary in the Department of Obstetrics and Gynecology, for her ever welcoming approach and enthusiasm to assist us in the secretarial work. Finally, we are indebted to card room workers of the respective hospitals for assisting in the chart retrival activity.

# **REFERENCES**

- 1. Growdon WB., Laufer MR. Ovarian and Fallopian Tube Torsion. June 2, 2011; March 20, 2012; http://www.uptodate.com/contents/ovarian and fallopian tube torsion
- 2. Bouguizane S, Bibi H, Farhat Y, Dhifallah S, Darraji F, Hidar S, et al. Adnexal torsion: a report of 135 cases. J Gynecol Obstet Biol Reprod 2003; 32(6):535-40.
- 3. Debra H. Ovarian Torsion: A Fifteen-Year Review. American College of Emergency Physicians 2001; 38 (2):156-9.
- 4. Hoffman L. Pelvic Mass In: Schorge O, Schaffer I, Halvorson M, Hoffman L, Bradshaw D, Cunningham F. (eds), Williams Gynecology, New York, The McGraw-Hill Companies, Inc,2008.
- 5. Varras M, Tsikini A, Polyzos D, et al. Uterine adnexal torsion. Pathologic and gray-scale ultrasonographic findings.Clin Exp Obstet Gynecol 2004;31(1):34-8.
- 6. Fleischer C. Ovarian Torsion. Sep 26, 2011 to Mar 23, 2012; http://www.emedicine.medscape.com/article/ovarian torsion to be omitted.
- 7. Way S. Ovarian cystectomy of twisted cysts. Lancet 1946; 2:46-7.
- 8. Albayram F, Hamper UM. Ovarian and adnexal torsion. Spectrum of sonographic findings with pathologic correlation J Ultrasound Med 2001;20(10):1083-89.
- 9. Argenta PA, Yeagley TJ, Ott G, Sondheimer SJ. Torsion of the uterine adnexa. Pathologic correlations and current management trends. J Reprod Med 2000;45(10):831-36.
- Bayer AI, Wiskind AK. Adnexal torsion: can the adnexa be saved? Am J Obstet\_Gynecol 1994;171(6):1506-10.

- 11. Gorkemli H, Camus M, Clasen K. Adnexal torsion after gonadotrophin ovulation induction for IVF or ICSI and its conservative treatment. Arch Gynecol Obstet 2002;267(1):4-6.
- 12. Haskins T, Shull BL. Adnexal torsion. South Med J 1986; 79:576-77.
- 13. Hibbard LT. Adnexal torsion.Am J Obstet Gynecol 1985; 152:456-61.
- 14. Rock, John A. Jones, Howard W. TeLinde's Operative Gynecology, Philadelphia, Lippincott Williams & Wilkins, 2008, 10th ed, 637-38.
- 15. Berek, Jonathan S. Berek & Novak's Gynecology, 14th Edition, Philadelphia: Lippincott Williams & Wilkins, 2007, 14<sup>th</sup>ed, 482.
- 16. Promecene PA. Laparoscopy in gynecologic emergencies. Semin Laparosc Surg 2002; 9(1): 64-75.
- 17. Harkins G. Ovarian torsion treated with untwisting: second look 36 hours after untwisting. J Minim Invasive Gynecol 2007; 14:270.
- 18. Shalev E, Bustan M, Yarom I, Peleg D. Recovery of ovarian function after laparoscopic detorsion. Hum Reprod 1995;10(11):2965-66.
- 19. Anders JF, Powell EC. Urgency of evaluation and outcome of acute ovarian torsion in pediatric patients. Arch Pediatr Adolesc Med 2005;159(6):532-35.
- 20. Aziz D, Davis V, Allen L, Langer JC. Ovarian torsion in children: is oophorectomy necessary? J Pediatr Surg 2004; 39(5):750-53.
- 21. McGovern PG, Noah R, Koenigsberg R, Little AB. Adnexal torsion and pulmonary embolism: case report and review of the literature. Obstet Gynecol Surv 1999;54(9):601-8.
- 22. Oelsner G, Cohen SB, Soriano D, Admon D, Mashiach S, Carp H. Minimal surgery for the twisted ischaemic adnexa can preserve ovarian function. Hum Reprod 2003;18(12):2599-602.
- 23. Rody A, Jackisch C, Klockenbusch W, Heinig J, Coenen-Worch V, Schneider HP. The conservative management of adnexal torsion--a case-report and review of the literature. Eur J Obstet Gynecol Reprod Biol 2002;101 (1):83-6.
- 24. Zweizig S, Perron J, Grubb D, Mishell DR. Conservative management of adnexal torsion. Am J Obstet Gynecol 1993;168(6.1):1781-95.
- 25. Sommerville M, Grimes DA, Koonings PP, Campbell K .Ovarian neoplasms and the risk of adnexal torsion. Am J Obstet Gynecol 1991;164(2):577-8.
- 26. McHutchinson LL, Koonings PP, Ballard CA, d'Ablaing G. Preservation of ovarian tissue in adnexal torsion with fluorescein. Am J Obstet Gynecol1993 May;168(5):1386-88.

#### **ORIGINAL ARTICLE**

# MATERNAL AND PERINATAL OUTCOME OF PREGNANCIES WITH PRETERM PREMATURE RUPTURE OF MEMBRANES (PPROM) AT TIKUR ANBESSA SPECIALIZED TEACHING HOSPITAL, ADDIS ABABA, ETHIOPIA

Biniyam Sirak (MD)<sup>1</sup>, Eyasu Mesfin (MD)<sup>1</sup>

# **ABSTRACT**

Introduction: Preterm premature rupture of membranes is a common complication of pregnancy associated with significant maternal, fetal and neonatal risks. An understanding of its magnitude and consequences is critical in providing appropriate intervention to prevent poor pregnancy outcomes.

**Objective:** To describe maternal and perinatal outcomes of preterm premature rupture of membranes at Tikur Anbessa Hospital, Addis Ababa, Ethiopia.

*Methodology*: A Retrospective cross-sectional descriptive study done at Tikur Anbessa Hospital from June, 2010 G.C. to June, 2013 G.C.

Results: The prevalence of preterm premature rupture of membranes in this study was 1.4%. Intra-amniotic infection, seen in 31.5% (35/111), was the commonest maternal complication. The mean latency period from rupture of membranes to delivery was 6.6 days. Twenty-six (23.2%) neonates were delivered by cesarean section. There were a total of 12 perinatal deaths, 4 (3.6%) stillbirths (2 antepartum and 2 itrapartum) and 8 (7.1%) early neonatal deaths, making the gross perinatal mortality rate to be 107 per 1000 live births. Prematurity was the commonest cause of neonatal death.

Conclusion and recommendations: Although the prevalence of preterm premature rupture of membranes in this study appears lower than many prior reports, the level of maternal and perinatal morbidity is high compared to many prior reports from similar setups. Especially the proportion of mothers presenting with established chorioamnionitis is high. Therefore, it is important that women be well informed regarding maternal, fetal and neonatal complications of premature rupture of membranes so that proper and timely management is provided.

Key words: PROM, Pre-term PROM, PPROM, Chorioamnionitis

# INTRODUCTION

Premature rupture of membranes (PROM) is defined as spontaneous rupture of membrane before onset of labor. Membrane rupture that occurs between the gestational ages (GA) of 28 and 37 completed weeks is referred to as preterm PROM (PPROM). PPROM occurs in 1%–3% of all pregnancies and is responsible for approximately one third of all preterm births (1-3). Latency period, the time from membrane rupture until delivery, is inversely correlated with the gestational age at membrane rupture. Regardless of management or clinical presentation, birth within 1 week is the most likely outcome of any patient with PPROM. A review of 13 randomized trials reported

that approximately 75% of patients with preterm PROM who were managed expectantly delivered within 1 week (4).

PPROM is associated with significantly increased risk of maternal, fetal and neonatal morbidity and mortality resulting from associated complications. Among women with preterm PROM, clinically evident intraamniotic infection occurs in approximately 15–25% (5). Abruptio placentae can cause PROM or occur subsequent to membrane rupture and affects 4% to 12% of these pregnancies (6). The frequency and severity of neonatal complications after PROM vary inversely with gestational age at membrane rupture and at delivery. The rates of these complications are higher in the setting of chorioamnionitis (7).

<sup>&</sup>lt;sup>1</sup>Department of Obstetrics & Gynecology, Addis Ababa University, Addis Ababa, Ethiopia

Management of PROM is primarily dependent on gestational age and the presence of complicating factors. It requires evaluation of the risks and benefits of expectant management or expeditious delivery. In expectant management of PPROM adjuvant antibiotic and corticosteroid therapy are widely shown to reduce GA-dependent and infectious complications significantly improving perinatal outcome. A Cochrane review of 22 placebo-controlled randomized trials involving 6800 women showed the benefits of using antibiotics following PPROM (5). According to the review; the use of antibiotics was associated with a statistically significant reduction in chorioamnionitis (RR 0.57, 95%; CI 0.37 to 0.86) and neonatal infections (RR 0.68, 95% CI 0.53 to 0.87). There was a reduction in the numbers of babies born within 48 hours (RR 0.71, 95% CI 0.58 to 0.87) and seven days of rupture of membrane (RR 0.80, 95% CI 0.71 to 0.90). In addition, a metaanalysis regarding antenatal corticosteroid administration after PPROM has confirmed steroid therapy to significantly reduce the risks for Respiratory Distress Syndrome (RDS) (20% versus 35.4%), Intra Ventricular Hemorrhage (IVH) (7.5% versus 15.9%), and necrotizing enterocolitis (0.8% versus 4.6%) (8).

Understanding the magnitude and consequences of Preterm PROM is vital in providing appropriate intervention to prevent poor pregnancy outcomes. Information regarding PPROM in Ethiopian setup, however, is very limited. The 2011 Ethiopia Demographic and Health Survey (EDHS) revealed complications of preterm birth, intrapartum related events, and sepsis and meningitis to be the leading causes of neonatal deaths in the country. The survey also showed that only about one-fifth (22 percent) of pregnant women were informed of vaginal gush or fluid as signs of pregnancy complications during their ante natal care (ANC) follow up (9).

This study was conducted at Tikur Anbessa Specialized Teaching Hospital where PPROM is managed following a management protocol prepared based on the current global recommendations and practice. According to the management protocol, all pregnant women with PPROM are admitted either for expectant management or immediate delivery. The study is designed primarily to give a baseline description of perinatal and maternal outcomes of PPROM cases.

# **SUBJECTS AND METHODS**

This is a hospital based retrospective cross sectional descriptive study done from June, 2010 G.C. to June, 2013 G.C. at Tikur Anbessa Hospital (TAH), a specialized central referral Hospital, Addis Ababa, Ethiopia. All mothers admitted to the Hospital with a diagnosis of PPROM during the study period were included. Their medical record numbers (MRN) identified from admission log books in the maternity ward and neonatal intensive care unit (ICU) were used to retrieve medical records/charts. Data was collected by the investigator using a pre-tested questionnaire from medical records of the study participants. Data was cleared prior to entry and data analysis was made using SPSS version 20.0 soft ware. Summary tables and charts were used for describing data.

Ethical clearance was obtained from the research and publication committee of the department of Obstetrics & Gynecology and IRB of Addis Ababa University. Permission was also obtained from the Hospital to access the medical records of mothers included in the study.

# **RESULT**

During the three years study period, a total of 8,283 mothers delivered in the study hospital. A total of 111 mothers (1 twin) had pregnancies complicated with Preterm PROM and gave birth to 112 neonates. The overall prevalence of Preterm PROM was 1.4% (111 / 8,283). The age of the study subjects ranged from 15-to-39 years while the mean age was 26.31 years. Majority were married, housewives, and from outside of Addis Ababa with proportions of 96.4% (107/111), 67% (75/111) and 82% (91/111) respectively. (Table-1)

| Table 1: Socio demographic characteristics of mothers with PPROM at TAH, from June, 2010 G.C. to June, 2013 |
|---|
| G.C. (n=111)  |

|                | Characteristics       | Frequency  | Percentage (n=111) |
|----------------|-----------------------|--|--------------------|
| Age            | 15-19                 | 4  | 3.6%               |
|                | 20-24                 | 36   | 32.4%              |
|                | 25-29                 | 37   | 33.3%              |
|                | 30-34                 | 24   | 21.6%              |
|                | 35-39                 | 10   | 9%                 |
|                | $\geq$ 40             | 0  | -                  |
| Address        | Addis Ababa           | 91   | 82%                |
|                | Out of Addis Ababa    | 20   | 18%                |
| Marital Status | Married               | 107  | 96.4%              |
|                | Single                | 4  | 3.6%               |
| Occupation     | House Wife            | 4<br>36<br>37<br>24<br>10<br>0<br>91<br>20<br>107<br>4<br>75 | 67.6%              |
| •              | Governmental Employee | 17   | 15.3%              |
|                | Private Employee      | 7  | 6.3%               |
|                | Student               | 6  | 5.4%               |
|                | Daily Laborer         | 4  | 3.6%               |
|                | Others                | 2  | 1.8%               |

Fifty three percent (59/111) were nulliparous. All except one (110/111) had ANC follow up. Health centers and Tikur Anbessa Hospital were the sites of ANC follow up for 54.5% (60/111) and 24.5% (27/111) of the mothers respectively. Information on danger signs of pregnancy was given to 81.8% (90/111) of the mothers during their ANC follow up. The mean gestational age at ROM was 33.83 weeks (SD of 2.4).

The ROM occurred at less than 34 weeks in 41.4% (46/111), and between 34 and 37 weeks in 58.6% (65/111) of the mothers. Fetal presentation at the time of admission was cephalic, breech and shoulder in 80.4% (90/112), 14.3% (16/112) and 5.4% (6/112) of the fetuses respectively. (See Table-2 below)

Prophylactic antibiotics were administered to 84 % (93/111) of the mothers. In addition, dexamethasone was administered in 87 % (40/46) of the mothers with ROM at less than 34 weeks. There was no documented use of tocolysis in the study group.

*Time of Delivery:* The mean gestational age at delivery was 34.57 weeks (SD of 2.2). Majority, 61.3% (68/111), gave birth at gestational age of ≥34 weeks but <37 weeks. The mean latency period from PROM to onset of labor was 6.6 days with a median of 3.0 and range of 1-65 days. Twenty four percent (27/112) of the neonates were born within the first day while 46.4% (52/112) were born with in the first week of rupture of membrane. One case of PPROM was admitted at GA of 29 weeks with GA at ROM of

27 weeks. She ultimately delivered at 37 weeks, after a latency period of 65 days, by Cesarean Section (C/S) for failed induction with an outcome of a female neonate weighing 2,880 grams and APGAR score of 8 and 9 in the first and fifth minutes. Excluding this outlier case; the mean, median and range of the latency period becomes 6.08, 3 (SD of 8.01 days) and 1-47 days respectively.

Mode of Delivery: Labor started spontaneously in 58.5% (65/111) of the mothers. Pregnancy was terminated by induction in 30.6% (34/111) and cesarean section before onset of labor in 10.8% (12/111). Indications for termination of pregnancy were chorioamnionitis, anticipated fetal lung maturity because of GA considered to be near term, confirmed lung maturity by amniocentesis and NRBPP in 54.3% (25/46), 21.7% (10/46), 17.4% (8/46) and 6.5%(3/46) respectively. The cesarean section delivery rate in the study group was 23.2% (26/112). Failed induction, chorioamnionitis with breech presentation and chorioamnionitis with previous caesarian scar were the main indications for C/S each accounting for 19.2% (5/26), 19.2% (5/26) and 15.3% (4/26) of cesarean deliveries respectively. The other indications include; shoulder presentation, footling breech, non reassuring biophysical profile (NRBPP), non reassuring fetal heart rate pattern (NRFHRP) and prolonged latent stage of labor with breech presentation in 11.5% (3/26), 11.5% (3/26), 11.5% (3/26), 7.7% (2/26) and 3.8% (1/26) of the cesarean deliveries respectively. (Table -3)

Table 2: Obstetric characteristics of mothers with PPROM at TAH, from June, 2010 G.C. to June, 2013 G.C. (n=111)

| Characteristics                   | Frequency | Percentage, % |  |
|-----------------------------------|-----------|---------------|--|
| Parity (n=111)                    |           |               |  |
| Nuliparous                        | 59        | 53.2          |  |
| Multiparous                       | 52        | 46.8          |  |
| GA at rupture of membrane (n=111) |           |               |  |
| < 34weeks                         | 46        | 41.4          |  |
| ≥ 34weeks                         | 65        | 58.6          |  |
| ANC follow up (n=111)             |           |               |  |
| Yes                               |           |               |  |
| At health centre                  | 60        | 54.1          |  |
| At Tikur Anbessa Hospital         | 27        | 24.3          |  |
| At private facility               | 15        | 13.5          |  |
| Other governmental hospital       | 8         | 7.2           |  |
| Sub total                         | 110       | 99.1          |  |
| No                                | 1         | 0.9           |  |
| Type of pregnancy (n=111)         |           |               |  |
| Singleton                         | 110       | 99.1          |  |
| Twin                              | 1         | 0.9           |  |
| Fetal presentation (n=112)        |           |               |  |
| Cephalic                          | 90        | 80.4          |  |
| Breech                            | 16        | 14.3          |  |
| Shoulder                          | 6         | 5.4           |  |

*Maternal Morbidity:* Clinical chorioamnionitis, seen in 31.5% (35/111) of the mothers, was the commonest maternal complication. Twenty five (22.5%) mothers presented with clinical chorioamnionitis, while additional 10 (9%) developed chorioamnionitis after admission. Puerperal endomyometritis, superficial abdominal wound infection and sepsis occurred in 13.5% (15/111), 4.5% (5/111) and 2.7% (3/111) of cases. There were no reported cases of maternal mortality or long term morbidity.

A multivariate binary logistic regression analysis showed statistical significant association between prophylactic antibiotic administration and Chorioamnionitis. Those who were not given prophylactic antibiotic had 339 times increased risk of developing chorioamnionitis (AOR 339.73 (95% CI: 31.09-3712.46). (Tables 3 and 4)

Table 3: Maternal outcome of mothers with PPROM at TAH, from June, 2010 G.C. to June, 2013 G.C.

| Characteristics  | Frequency | Percentage (%) |  |
|--|-----------|----------------|--|
| Gestational age at delivery (n=111)                      |           |                |  |
| ≥ 28 weeks and < 34 weeks                                | 37        | 33.3           |  |
| $\geq$ 34 weeks and $<$ 37 weeks                         | 68        | 61.3           |  |
| ≥ 37 weeks   | 6         | 5.4            |  |
| Mode of delivery (n=112)                                 |           |                |  |
| Vaginal  | 86        | 76.8           |  |
| Cesarean section   | 26        | 23.2           |  |
| Indication for cesarean section (n=26)                   |           |                |  |
| Failed induction   | 5         | 19.2           |  |
| Chorioamnionitis with breech presentation                | 5         | 19.2           |  |
| Chorioamnionitis with previous C/S                       | 4         | 15.3           |  |
| Shoulder presentation in labor                           | 3         | 11.5           |  |
| Footling breech  | 3         | 11.5           |  |
| Non reassuring biophysical profile (NRBPP)               | 3         | 11.5           |  |
| Non reassuring fetal heart rate pattern (NRFHRP)         | 2         | 7.7            |  |
| Prolonged latent stage of labor with breech presentation | 1         | 3.8            |  |
| Maternal morbidity (n=111)                               |           |                |  |
| Clinical chorioamnionitis                                | 35        | 31.5           |  |
| Puerperal endomyometritis                                | 5         | 4.5            |  |
| Sepsis   | 3         | 2.7            |  |

Perinatal Outcome: A total of 112 neonates, 57 (50.9%) males and 55 (49.1%) females, were born. The mean birth weight of the neonates was 2,315 grams (SD of 558.5). Fifty percent (56/112) weighed 1500 - 2500 grams while 39.3% (44/112), 8% (9/112) and 2.7% (3/112) weighed >2500 grams, 1000 - 1499 grams and < 1000 grams respectively. The APGAR score at the first and fifth minutes was less than seven in 23.2% (26/112) and 5.4% (6/112) of the neonates respectively. The rate of admission to neonatal ICU was 48.2% (54/112). There were a total of 12 perinatal deaths out of the 112 births; 4 being stillbirths (2 antepartum and 2 intrapartum) and 8 early neonatal deaths. The gross perinatal mortality rate, hence, was 107 per 1000 live births. Most of the perinatal deaths had birth weight of <2500grams and GA at ROM of <34 weeks with proportions of 92% (11/12) and 75% (9/12) respectively. (Table -5).

Prematurity was the commonest stated reason for the perinatal mortality accounting for 66.7% (8/12) of perinatal deaths. Other stated causes include congenital anomaly, birth asphyxia and intra uterine growth restriction (IUGR) accounting for 16.7% (2/12), 8.3% (1/12) and 8.3% (1/12) respectively. A multivariate binary logistic regression analysis showed statistical significant association between GA at rupture of membrane and APGAR score at five minutes, and perinatal outcome. Rupture of membrane at <34 weeks of gestation had five times higher risk of being dead on discharge from the hospital AOR 5.03 (95% CI: 1.28-19.76). APGAR score of <7 was also seen to have seventy times higher risk of being dead on discharge from the hospital AOR 70.00 (95% CI: 7.16-684.24).

Table 4: Multivariate binary logistic regression analysis of Selected Variables with Chorioamnionitis of mothers with PPROM at TAH, from June, 2010 G.C. to June, 2013 G.C.

| Chorioamnionitis           |             |    |     |        |                 |
|----------------------------|-------------|----|-----|--------|-----------------|
| Selected Variables         |             | no | yes | AOR    | 95% CI          |
| GA <34 and GA >=34         | <34 weeks   | 27 | 20  | 2.99   | .72-18.43       |
|                            | >= 34 weeks | 50 | 15  |        |                 |
| Administration of Prophy-  |             |    |     |        |                 |
| lactic Antibiotics to the  | yes         | 74 | 19  | 339.73 | 31.09-3712.46** |
| Mother                     | no          | 2  | 16  |        |                 |
| Corticosteroid administra- | yes         | 24 | 16  | 8.55   | 1.42-51.45**    |
| tion to the Mother         | no          | 52 | 19  |        |                 |
| Onset of Labor             | Spontaneous | 54 | 13  |        |                 |
|                            | Induced     | 18 | 15  | 7.98   | 1.73-36.82**    |

AOR= Adjusted Odds Ratio, CI= Confidence Interval, \*\*Statistically Significant Adjusted for Gestational Age, Informed about danger sign, Marital Status, and Address of the Mother

Table 5: Perinatal outcome of mothers with PPROM at TAH, from June, 2010 G.C. to June, 2013 G.C. (n=112)

| Characteristics       | Frequency | Percentage (%)<br>n=112 |  |
|-----------------------|-----------|-------------------------|--|
| Sex                   |           |                         |  |
| Male                  | 37        | 33.3                    |  |
| Female                | 6         | 5.4                     |  |
| Birth weight in grams |           |                         |  |
| <1,000                | 3         | 2.7                     |  |
| 1,000 – 1,499         | 9         | 8.0                     |  |
| 1,500 - 2,499         | 56        | 50                      |  |
| <sup>3</sup> 2,500    | 44        | 39.3                    |  |
| APGAR score           |           |                         |  |
| First minute          |           |                         |  |
| < 7                   | 26        | 23.2                    |  |
| <sup>3</sup> 7        | 86        | 76.8                    |  |
| Fifth minute          |           |                         |  |
| < 7                   | 6         | 5.4                     |  |
| <sup>3</sup> 7        | 106       | 94.6                    |  |
| NICU admission        |           |                         |  |
| Yes                   | 54        | 48.2                    |  |
| No                    | 58        | 51.8                    |  |
| Perinatal outcome     |           |                         |  |
| Still born            | 4         | 3.6                     |  |
| Early neonatal death  | 8         | 7.1                     |  |
| Alive on discharge    | 100       | 89.3                    |  |

# **DISCUSSION**

Preterm PROM, occurring globally in 1%-3% of all pregnancies, is associated with significant maternal, fetal and neonatal risks. The 1.4% prevalence of PPROM in this study is generally with in the global range. However, it is significantly lower than reported prevalences from similar developing countries including that of Nigeria and Pakistan with reported prevalences of 3.3% and 16% respectively (10, 11). Compared to prior local reports, it is higher than the prevalence of 0.9% in the study done at three teaching hospitals TAH, St Paul's Hospital (SPH) and Gandhi Memorial Hospital (GMH) in the year 2007 (12). It, however, is lower than the reported prevalence in the study at SPH and TAH which are 7.5% of women age <35yrs and 12.6% of women age>/=35yrs in a period of 21 months (13). The local reported prevalence of PPROM appears widely variable despite similar study methodology and setup.

There is currently no effective way of preventing most preterm PROMs as it is mostly unpredictable. However, its early and accurate diagnosis would allow for gestational age-specific obstetric interventions designed to optimize maternal and perinatal outcome, and minimize serious complications (3). It is therefore important that all pregnant women be well informed regarding maternal, fetal and neonatal complications, and the need to immediately seek medical care when it occurs. In our study, although nearly all the study mothers had ANC follow-up, only 81.8% (90/111) were told about danger signs of pregnancy during their follow up. This finding still is much higher than the national reported figure of only 22 percent (2011 EDHS) (7). This could be due to the fact that this study was done at a tertiary university hospital where most of the clients are from Addis Ababa with better access to ANC and information.

The management of pregnancies complicated with preterm PROM, is individualized, highly controversial and challenging. Administration of adjunctive prophylactic antibiotics is one of the interventions known to improve obstetric outcome. The goal of antibiotic therapy is to reduce the frequency of maternal and fetal infection and delay the onset of preterm labor (ie, prolong latency period). The mean latency period from PPROM to delivery in our study was 6.6 days, and 46.8% of the neonates were born within the first week of rupture of membrane. This latency period in

this study is better than a previously reported latency period in a review of 13 randomized trials involving PPROM cases managed expectantly where 75% of patients delivered within 1 week (14).

The risk of clinically evident infection is significant following PPROM. Intraamniotic infection was the commonest maternal complication of PPROM in this study. The infection rate of 31.5% (35/111) was comparable to the reported prevalence of 32.7% in the study done in the same set up in 2007 but much higher than the infection rate of 13.9 percent reported in the Nigerian study (10, 12). This high level of maternal morbidity could be due to significant number of mothers in this study who came to the study hospitals with already established chorioamnionitis 22.5% (25/111). Many of these cases could have been prevented had they come to the facility earlier as soon as ROM occurs

Caesarean section rate was 23.2 % for this study. This is comparable to a rate of 23.1% reported in the study done in the three teaching hospitals TAH, SPH and GMH but higher than the 14% rate reported in Ayub medical college, Abbottabad, Pakistan (11).

The most significant risks to the fetus after preterm PROM are complications of prematurity. Similarly, the most common complication of PROM related to perinatal outcome in this study was prematurity and its side effect. The perinatal mortality rate of 98.2 per 1000 births in this study, as a result, is more than twice higher than the national overall perinatal mortality rate of 46 per 1,000 pregnancies reported in DHS-2011 (7). The finding, however, is comparable to reported perinatal mortality rate of 89/1000 in the Nigerian study and reported rate of 105/1000 in other prior studies (10, 15).

The major limitation of this study was the restriction of the study population to a central referral hospital with a selected group of women. In addition, it is a small scale retrospective study and it was not possible to assess risk factors associated with PPROM because of incomplete information in the medical records. Hence the findings of this study may not reflect the true situation in the general population and should be interpreted with caution. Despite the limitations, this study has provided baseline information on PPROM in our setup and is a stepping stone towards further research on PPROM among Ethiopian women.

Conclusion and Recommendation: Although the prevalence of PPROM in this study appears lower than many prior reports, the level of maternal and

perinatal morbidity is high compared to reports from similar setups. Intraamniotic infection and prematurity with its side effects were the commonest maternal and perinatal complications of PPROM respectively in this study. The proportion of mothers presenting with established chorioamnionitis was high contributing to the high intraamniotic infection rate. It is, therefore, important that all pregnant women be well informed regarding potential complications of PPROM during their ANC follow to avoid delay in presentation.

The practice of antibiotic administration during management of Preterm PROM should be encouraged as significant reduction in chorioamnionitis was seen in agreement with most other prior studies. To obtain more representative information on PPROM among Ethiopian women and come up with more reliable recommendations further large scale prospective research is recommended.

#### REFERENCES

- 1. Meis PJ, Ernest JM, Moore ML. Causes of low birth weight births in public and private patients. *Am J Obstet Gynecol*. 1987;156:1165–8.
- 2. Tucker JM, Goldenberg RL, Davis RO, et al: Etiologies of preterm birth in an indigent population: is prevention a logical expectation?. *Obstet Gynecol* 1991; 77:343.
- 3. Premature rupture of membranes. ACOG Technical Bulletin 115. Washington, DC: American College of Obstetricians and Gynecologists; 1998.
- 4. Mercer BM, Arheart KL. Antimicrobial therapy in expectant management of preterm premature rupture of the membranes. Lancet 1995;346:1271-1279
- 5. Kenyon S, Boulvain M, Neilson JP. Antibiotics for preterm rupture of membranes. Cochrane Database of Systematic Reviews 2010, Issue 8. Art. No.: CD001058. DOI: 10.1002/14651858.CD001058.pub2. (Metaanalysis)
- 6. Gonen R, Hannah ME, Milligan JE: Does prolonged preterm premature rupture of the membranes predispose to abruptio placentae? Obstet Gynecol, 1989; 74:347.
- 7. Soraisham AS, Singhal N, McMillan DD, et al. A multicenter study on the clinical outcome of chorioamnionitis in preterm infants. Am J Obstet Gynecol 2009; 200:372.e1.
- 8. Harding JE, et al, Do antenatal corticosteroids help in the setting of preterm rupture of membranes? Am J Obstet Gynecol, 2001; 184:131.
- 9. Central Statistical Agency [Ethiopia] and ICF International (2012) Ethiopia Demographic and Health Survey 2011. Central Statistical Agency and ICF International, Addis Ababa, Ethiopia and Calverton, Maryland.
- 10. Adetunji O. Adeniji and Oluseyi. O. A. Atanda, Interventions and Neonatal Outcomes in Patients with PROM at and beyond 34 weeks Gestational Age at Tertiary Health Facility in Nigeria. British Journal of Medicine and Medical Research 2013, 3(4); 1388-1397.
- 11. Shehla Noor, et al. Fetomaternal Outcome in patients with or without Premature Rupture of Membranes, Department of Obstetrics and Gynaecology, Pathology, Medicine, Ayub Medical College, Abbottabad, Pakistan, J Ayub Med Coll Abbottabad 2010; 22(1).
- 12. Dereje Kebede and Lukman Yusuf: Perinatal and Maternal outcome of Preterm Premature Rupture of Membranes in three teaching hospitals of Addis Ababa University Medical Faculty, Department of Obstetrics and Gynaecology; December 2007.
- 13. W. Maraz and Z. Lakew, Pregnancy outcome in the elderly gravida in Addis Ababa, East African Medical Journal Vol. 79, No 1 January 2002.
- 14. Garite TJ, Freeman RK: Chorioamnionitis in the preterm gestation. Obstet Gynecol, 1982; 59:539.
- 15. Padma Shukla, Meena Bhargava, Disha. "Study of Maternal and Fetal Outcome in Preterm Premature Rupture of Membrane". Journal of Evolution of Medical and Dental Sciences 2014; Vol. 3, Issue 07, February 17; Page: 1789-1795, DOI: 10.14260/jemds/ 2014/2059.

Amir Adem, Sintayehu Abebe, Abraha Hailu, Bethlehem Feleke, Meseret Berhe, Merhawit Atsibeha, Victor G Davilla. *Ethiop Med J*, 2014, Vol. 52, No. 4

#### **ORIGINAL ARTICLE**

# HEART DISEASES IN NORTH ETHIOPIA PATTERN OF ECHOCARDIOGRAPHIC ABNORMALITIES AMONG ADULT CARDIAC PATIENTS - AN EXPERIENCE FROM AYDER HOSPITAL OF MEKELLE UNIVERSITY

Amir Adem<sup>1</sup>, Sintayehu Abebe<sup>1</sup>, Abraha Hailu<sup>1</sup>, Bethlehem Feleke<sup>1</sup>, Meseret Berhe<sup>1</sup>, Merhawit Atsibeha<sup>1</sup>, Victor G Davilla<sup>2</sup>

# **ABSTRACT**

**Background:** Cardiovascular diseases are leading causes of mortality worldwide. Specific etiologies vary in different regions and these variations are explained by the concept of Epidemiologic transition.

**Objectives:** To describe the pattern of echocardiographically detected cardiac diseases among patients who presented to Cardiac clinic of Ayder referral hospital and to analyze associations of cardiac diseases with age and economic status.

**Methods:** A retrospective review of records of adult patients who had echocardiographic study at Cardiac Clinic of Ayder referral hospital from September 2011 to June 2013 was made. The collected data was analyzed using SPSS Version 21.

**Results:** Total of 1028 echocardiograms were reviewed. The mean age of the patients was 50.6 (sd =18.7) years with male to female ratio of 0.93. Commonest echocardiographic abnormality was Valvular heart disease (44.6%), with rheumatic in younger and degenerative etiologies in older age groups. Diastolic heart failure accounted for 31.9% of abnormal studies, 60.4% of which were ascribed to hypertensive heart disease. Pulmonary hypertension of any etiology was diagnosed in 32.6% of the cases. Among patients with rheumatic heart diseases, co-occurrence of Mitral and Aortic valve disease was the commonest.

**Conclusion:** Valvular disease was the most common echocardiographic finding among adult cardiac patients in the study area.

Key words: Echocardiography in Ethiopia, Heart diseases Ethiopia

#### INTRODUCTION

Cardiovascular diseases are major causes of morbidity and leading cause of death in the world accounting for 30% of the latter by 2008. They contribute to nearly 40% of all-cause mortality in high-income countries and about 28% in low- and middle-income countries[1,2]. The highest rate adjusted mortality rates are seen in low and middle income countries, though trending data for most African countries is not available [3]. The rate of cardiovascular disease is increasing in the developing world and many people in low and middle income countries die younger from cardiovascular diseases often in their most pro-

ductive years. This deaths at early age are said to be due to a high risk of exposure to risk factors such as tobacco, lack of prevention programs in comparison to people in high income countries and lack of access to effective and equitable health care services[4].

Cardiovascular diseases are the leading causes of death in all developing regions of the world with the exception of sub-Saharan Africa, where the first phase of the epidemiologic transition is still dominant, although with a shifting trend towards a double burden of infectious and non-communicable diseases [5,6].

Prior reports from various African countries evidenced regional variations of common causes of heart diseases, with ample data suggesting major

<sup>1</sup>Department of Internal Medicine, College of Health Sciences, Mekelle University <sup>2</sup>Division of Cardiovascular Diseases, School of Medicine, Washington University *Corresponding author: amiradem@gmail.com* 

causes being still infections or cardiovascular complications of it.

In a prospective study among patients with cardiovascular diseases from Ghana, hypertensive heart disease followed by rheumatic heart disease were the commonest echocardiographically identified pathologies[7]. In another analysis of the clinical and echocardiographic features of all consecutive subjects presenting with heart failure in a tertiary institution in Abuja, Nigeria also showed untreated hypertension to be a leading cause of heart failure [8].

In comparison, a review of five hundred consecutive cardiological patients evaluated by echocardiography as a referral service in Mulago hospital, Uganda suggests that endomyocardial fibrosis may be the most common heart disease[9].

According to data obtained from the Sudan household survey (2006) hypertensive heart disease, rheumatic heart disease, ischemic heart disease and cardiomyopathy constitute more than 80% of cardiovascular diseases in Sudan[10].

A cross-sectional study from Jimma showed that rheumatic, hypertensive and cardiomyopathic heart diseases accounted for more than three-quarters of cardiac diseases in the study population[11]. A retrospective study conducted at pediatric cardiac clinic of Zewditu memorial hospital also showed dominance of rheumatic heart disease in a hospital setting[12].

In another review of the echocardiogram reports of 608 consecutive patients done from July 2009 to October 2011 in Enugu, South-East Nigeria, rheumatic heart disease (predominantly mitral valve regurgitation) was the commonest cardiac abnormality in adolescents and young adults. Degenerative valvular diseases and left ventricular diastolic dysfunction were the commonest abnormalities in the elderly. [13]

Yet in another study from Gondar among patients with cardiovascular diseases which were followed in the cardiac clinic of the Gondar College of Medical Science Hospital between 1985 and 1988, the commonest form of heart disease in Ethiopians was found to be rheumatic heart disease (42%), which affected mostly young people often with advanced valvular lesions. Hypertension (38.1%) was the second most common cause of heart disease.[14]

A recent publication of record review of patient registers for 3282 Ethiopian patients (from January 2001 to December 2012) with confirmed cardiovascular

disorders at adult cardiology clinic and neurology clinic of Tikur Anbessa specialized hospital also showed valvular heart disease to be the commonest cardiovascular disorder with dramatic increase of ischemic heart disease over the years[15]. Echocardiography permits accurate assessment of myocardial structure, function and perfusion [16] and thus is a non-invasive, relatively affordable and therefore an ideal tool to assess cardiac morbidities in developing countries[17,18].

Cardiovascular diseases are one of the commonest challenges in daily practice by clinicians in Ethiopia. Treating patients with heart diseases require greater expertise and hospital resources, therefore knowing the pattern of diseases can help in directing the bulk of the available resources to address the commonest pathologies. Despite this fact there are no prior published reports to our knowledge describing pattern of heart diseases in the geographic area we are reporting from.

The aim of this study is to assess the relative contribution of the various causes of cardiovascular morbidity in the study setting, which will help policy makers as a tool for decision making in allocating resources. Additionally it can be used as a baseline data for community based epidemiological studies to see burden of cardiovascular diseases in the public setting.

#### MATERIALS AND METHODS

This study was conducted at Ayder referral hospital of Mekelle University, Ethiopia. It is situated in Mekelle city, 783 KM north of Addis Ababa. Ayder is the teaching hospital of College of Health Sciences, Mekelle University and is the biggest tertiary referral hospital in Tigray regional state of Ethiopia. It serves the population of Tigray and neighboring regions of Afar and South eastern parts of Amhara, thus having a population of 8 million in its catchment area.

The hospital renders comprehensive patient care facility with various subspecialty level services. Among which the Cardiology unit under the department of Internal Medicine has been established ever since September 2011 building it's capacity to do various non-interventional and interventional Cardiology practices.

Study design and eligibility for the study: A retrospective record review was conducted to collect data registered from September 2011 to June 2013. The source population for the study was all adult patients presenting to Ayder referral hospital and the study population was patients who have undergone echocardiography in the cardiac clinic of the hospital. The echocardiography registry book of cardiology unit in Ayder referral hospital was entered in to a standardized Microsoft EXCEL table format by two trained nurses of the cardiology clinic, which was later used as a source of data for this study. Echocardiographic studies of all adult patients who had examination done in the study period at the cardiology clinic were enrolled in this review, thus their data extracted.

Patients with incomplete records and those with normal study were excluded. Pediatric and adolescent patients, who were defined as those 19 years of age or younger based on the World Health Organization (WHO) definition were also excluded from this study [19].

The registry includes age, sex and payment status, which were all used as independent variables. The dependent variable was the type of echocardiographic abnormality seen. The payment state of patients was indirectly used to infer the economic state. People who have low income, which was verified through local social justice systems at the time of sickness are issued fee waiver certificates by the local authorities [20], and are offered health care service including echocardiography for free. Thus patients who were registered to have received free medical care are considered to be the poorest among the society.

**Echocardiography:** In the hospital echocardiograms were performed using General Electronic's VIVID  $S_5$  and HP-Sonos 2000 machines by three trained Internists. Patients underwent transthoracic 2-D, M-Mode, Doppler studies (including Pulsed wave Doppler, Continuous wave Doppler, Color Doppler and Tissue Doppler) and few patients had transesophageal study when indicated. Echocardiographic studies were performed according to the American Society of Echocardiography standards[21].

Diagnosis of rheumatic heart disease (RHD) was made in the presence of typical echocardiographic rheumatic changes which are consistent with WHO and World Heart Federation's guidelines. [22-24]. Among patients with compatible clinical likelihood, if echocardiographic alular involvement favors degenerative changes, diagnosis of degenerative valve disease was made [25,26].

Mitral valve prolapse was diagnosed with systolic displacement (> 2 mm) of mitral leaflets into the left atrium, below the plane of the mitral annulus especially if leaflet was myxomatous[22]. The echocardiographic features typical of infective endocarditis and thus looked for were presence of vegetation, abscesses, new partial dehiscence of a prosthetic valves, or occurrence of new valvular regurgitation [22].

Dilated cardiomyopathy was diagnosed in the presence of Left ventricular or biventricular dilatation and concomitant systolic dysfunction[21,22]. The diagnosis of Ischemic heart disease was made using 2-D Sonographic analysis of the 16 segments (according to American society of echocardiography) to look for regional wall motion abnormalities. A hypertensive heart disease was diagnosed in the presence of concentric Left ventricular hypertrophy often with coexistent Diastolic dysfunction among known hypertensive patients [22].

Diagnosis of Diastolic dysfunction (Heart failure with preserved ejection fraction) (DD) was made using pulsed wave interrogation of transmitral flow coupled with Tissue doppler study of medial and lateral mitral annulus[22].

Pulmonary hypertension diagnosis was reached using Continuous wave Doppler tracings of Tricuspid regurgitation jet to estimate the systolic pressure gradient between right Ventricle and right Atrium using modified Bernoulli equation. Right atrial pressure was assumed to be 3-5mmhg and was then added to the pressure gradient to yield PASP. PASP> 35mmhg was used to define Pulmonary hypertension [22,27].

Diagnosis of possible Myocarditis was suggested in the presence of global Left Ventricular systolic dysfunction coupled with absent or minimal LV chamber dilatation [28]. Pericardial effusion was considered significant when there exists a persistent echofree space throughout the cardiac cycle. The M-mode and 2-D echocardiographic features of constrictive pericarditis and increased diastolic flow reversal with expiration in the hepatic vein were used to establish the diagnosis of constrictive pericarditis[22].

2-D echocardiography was used to look for congenital anatomical defects, shunts or Pulmonary valve morphological abnormalities, with Doppler studies to assess hemodynamic consequences and shunt assessment[22].

Statistical Methods: The collected data was computerized using SPSS version 21 and data cleaning was performed by the investigators running frequencies and cross-tabulations. From the cleaned data frequency and descriptive analysis was done. Associations with age, sex and payment status were sought using Pearson chi-square and ANOVA. P value  $\leq$  0.05 was considered statistically significant.

**Ethical consideration:** The proposal for this study is approved by the Institutional review board of College of Health sciences, Mekelle University. The results of this study shall be disseminated to the responsible bodies and the scientific community through publication in scientific journals.

# **RESULTS**

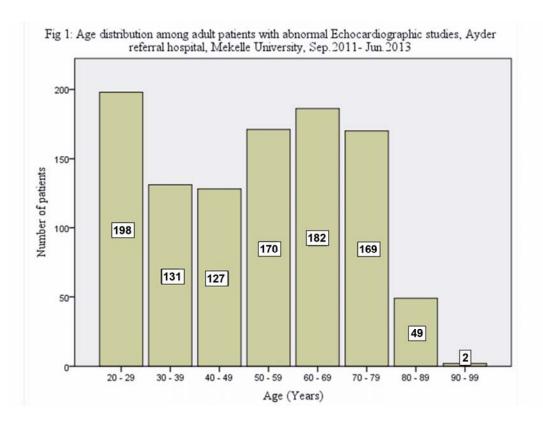
Total of 2056 patients were recorded, among whom 42 (2.0%) had incomplete registry, 7 (0.3%) and 3 (0.15%) patients lack age and payment status documentation respectively. Of the remaining 2004 pa-

tients 7 (0.3%) had Atrial fibrillation without structural heart disease and 666 (32.4%) of the patients had normal study. Additionally 303 (14.7%) patients were aged 19 years or less and were excluded. The final number of records analyzed was 1028.

Mean age in years of the patients was  $50.6\pm18.7$  (ranges from 20 to 98 years) and the median age was 52 years. Mean ages for male and female patients was  $51.8\pm18.9$  and  $49.5\pm18.5$  years respectively, with the women being younger. The age distribution among the patients was diverse. (Fig.1), Female patients account for 51.8% of the total. Payment status was recorded for all patients. Among all patients 62.7% were covering their medical bills, which for the purpose of this report were considered to be "not-poor" and the rest to be poor. No significant difference existed between men and women on payment status (p = 0.396) (Table 1).

Table 1: Sociodemographic characteristics of patients with abnormal Echocardiographic study, Ayder Referral Hospital, Mekelle University, Ethiopia. Sep. 2011 – Jun. 2013

| Variable                   | S               | ex              |
|----------------------------|-----------------|-----------------|
| Number (%)                 | Male Female     |                 |
| Age (Mean ± SD) Years      |                 |                 |
| Total $50.6 \pm 18.7$      | $51.8 \pm 18.9$ | $49.5 \pm 18.5$ |
| Payment status: Number (%) |                 |                 |
| Paying 645 (62.7%)         | 304 (61.4%)     | 341 (64.0%)     |
| Free 383 (37.3%)           | 191 (38.6%)     | 192 (36%)       |
| Total                      | 495(48.2%)      | 533(51.8%)      |



Commonest echocardiographic abnormalities were valvular heart disease, mainly, of Rheumatic etiology, followed by pulmonary hypertension and Diastolic dysfunction with or without Hypertensive heart disease, respectively. (Fig. 2). Mean ages for diagnosis of different Echocardiographic abnormalities was variable (p<0.001). (Fig. 3). Rheumatic heart disease was the commonest abnormality in the age group of 20-29 years, with Degenerative heart disease taking precedence in the elderly. (Table 2). Rheumatic heart disease, mainly, Mitral stenosis was more common in women and Diastolic dysfunction was more frequent in men. (Table 3).

Mean age in years for patients with Rheumatic heart disease was 33.01±11.6. Those with only Mitral Stenosis, Mitral Stenosis and Regurgitation and Mitral Regurgitation only had mean ages in year's

of32.8±9.7, 33.3±10.8 and34.2±14.5, respectively. For patients with Aortic valve disease, Multi-Valve disease, Severe Mitral Stenosis with mild Aortic Regurgitation and Mitral with Aortic Regurgitation mean ages were34.8±12.8 and 34.1±11.3, 29.9±9.9, 31.8±13.0 years respectively.

Male to female ratio among patients with Rheumatic Heart Diseases was 0.57(p<0.001), and for patients with Mitral Stenosis the ratio was 0.29 (p=0.026). (Table 3). Among patients with Rheumatic heart disease 61.6% occurred in paying patients, and no statistically significant difference was seen comparing paying and free patients (p=0.689).

Table 2: Frequency of most common echocardiographic abnormalities in different age groups. Ayder referral hospital, Mekelle University, Ethiopia. Sep.2011 – Jun.2013

| Diagnosis                       | 20-29 | 30-39 | 40-49 | 50-59 | 60-69 | 70+  |
|---------------------------------|-------|-------|-------|-------|-------|------|
| Rheumatic<br>Heart Dis-<br>ease | 54.4  | 40.5  | -     | -     | -     | -    |
| Pulmonary<br>hypertension       |       | 45.0  | 31.5  | 28.2  | -     | -    |
| Diastolic dysfunction           | -     | -     | 32.3  | 42.9  | 48.9  | 44.6 |
| Degenerative valve disease      | -     | -     | -     | -     | 29.1  | 59.0 |
| Hypertensive heart disease      | -     | -     | 29.9  | 29.4  | 35.2  | 34.8 |
| Pericardial diseases            | 12.1  | 14.3  | -     | -     | -     | -    |

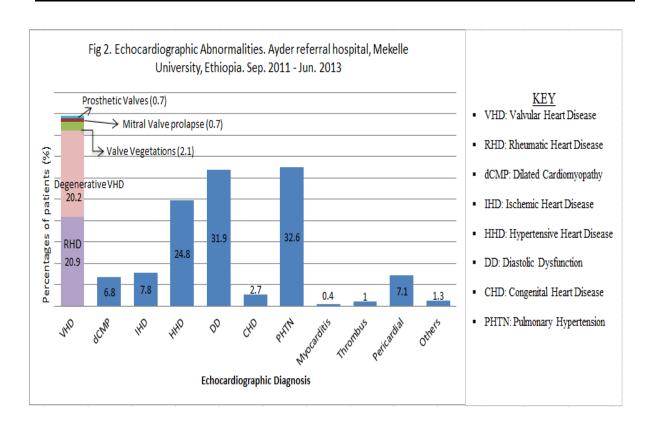


Table 3: Sex distribution among patients with common echocardiographic abnormalities seen in Ayder referral hospital, Mekelle University, Ethiopia. Sep.2011– Jun.2013

| Diagnosis   | Total number of patients | Male/Female ratio | p-value |
|---|--------------------------|-------------------|---------|
| Rheumatic heart disease                               | 215                      | 0.57              | < 0.001 |
| Mitral stenosis                                       | 18                       | 0.29              | 0.026   |
| Mitral stenosis and regurgitation                     | 35                       | 0.52              | 0.095   |
| Mitral regurgitation                                  | 13                       | 0.30              | 0.069   |
| Aortic stenosis and regurgitation                     | 14                       | 0.40              | 0.14    |
| Multivalve disease*                                   | 71                       | 0.73              | 0.303   |
| Severe Mitral stenosis and mild Aortic regurgitation§ | 23                       | 0.44              | 0.085   |
| Mitral and Aortic regurgitation§                      | 41                       | 0.75              | 0.48    |
| Degenerative valve diseases                           | 208                      | 0.77              | 0.135   |
| Ischemic heart disease                                | 81                       | 1.08              | 0.487   |
| Dilated cardiomyopathy                                | 70                       | 1.03              | 0.658   |
| Diastolic dysfunction                                 | 328                      | 1.16              | 0.016   |
| Congenital heart diseases                             | 28                       | 1.15              | 0.56    |
| Pericardial diseases                                  | 73                       | 1.28              | 0.155   |
| Pulmonary hypertension <sup>Ψ</sup>                   | 335                      | 0.71              | 0.003   |
| Hypertensive heart diseases                           | 255                      | 1.09              | 0.14    |
| Valve vegetations                                     | 22                       | 2.14              | 0.057   |
| Myocarditis   | 4                        | 0.25              | 0.353   |

<sup>\*</sup>Multivalve disease: Constitutes involvement of two or more valves excluding 0,8

Rheumatic heart disease was mainly seen to involve Mitral and Aortic valves. Pure Mitral regurgitation was documented in 6% and Mitral stenosis in 8% of patients. Isolated Mitral valve disease with combined stenotic and regurgitant physiology was seen in 16%, while isolated Aortic valve disease with stenotic and/or regurgitant physiology was found in 7% of cases. Nineteen percent of cases of rheumatic heart disease present with mixed regurgitant lesions of Aortic and Mitral valves. Severe Mitral stenosis with mild Aortic regurgitation was evident in 11%. Mixed valve lesions excluding the above mentioned combinations were seen in 33% of the cases.

The mean age of patients with Degenerative Valve Diseases was 67.4±11.4 years. Of this group of patients, Aortic valve involvement was documented in 95.7% of cases and isolated mitral valve lesions accounted for the rest (4.3%). Dilated Cardiomyopathy accounted for 6.8% of the cases, with mean age of the patients in this group being 50.0±16.5 years.

Ischemic Heart Disease was diagnosed in 7.8% of cases, at a mean age of 59.4±13.4 years and with more occurrence at higher age groups (p<0.001). The male to female ratio among this group was 1.1 with no statistically significant difference (p= 0.487). Of patients in this group 33.3% were being treated for free, and comparing with paying patients we found no statistically significant difference (p= 0.447).

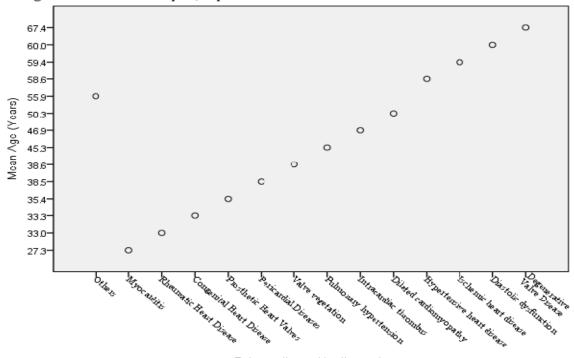
Hypertensive Heart Disease and Diastolic Dysfunction (Heart Failure with Preserved Systolic Function), were seen in 24.8% and 31.9% of our patients respectively. Only 78% of patients with echocardiographic diagnosis of Hypertensive heart disease were concomitantly diagnosed as having diastolic dysfunction. Documentation stating the different grades of diastolic dysfunction were not complete and thus not seen individually in this review. Mean age for patients with Hypertensive Heart Disease was 58.6±15.1 and for those with Diastolic Dysfunction was 60.0±14 years. Pericardial Diseases were seen in

<sup>&</sup>lt;sup>V</sup>Pulmonary hypertension in the above table is inclusive of all etiologies.

7.1% of our patients. Among these Constrictive pericarditis constituted 19.7%(14 patients), and occurred at a mean age of 41.4±16.1 years. Pulmonary Hypertension was diagnosed in 32.6% of cases and mean age was 45.3±18.8 years. The etiology for Pulmonary hypertension in these patients is varied with 69.4% accounted for by left sided heart failure. Among the rest, the mean age was 48.3±17.6 with male to female ratio of 1.02.

The mean age for patients presenting with Congenital Heart Diseases was 33.8±14.4 years and Atrial Septal Defects (46.4% of Congenital heart diseases) followed by Congenital Pulmonary stenosis (17.9%), Bicuspid Aortic valve (14.3%) and Ventricular Septal Defects (10.7%)were the most common anomalies. Mean (SD) ages for the diagnosis of these congenital anomalies were 36.5±15.3, 32.4±12.9, 41.8±19.5 and 21.7±1.5 years, respectively.

Fig 3: Age distribution among common echocardiographic abnormalities seen in Mekelle University College of health sciences hospital, Sep. 2011 – Jun 2013



Echocardiographic diagnosis

# **DISCUSSION**

In the current study, 44.6% of patients had Valvular Heart Disease, among whom Rheumatic Heart diseases account for 46.9% (216 patients) of the later. This figure is much lower than prior reports from Gondar and Jimma, which could be accounted for by variations in screening tools and the possible evolution of causes of cardiovascular morbidity and mortality with epidemiologic transition[5,11,14]. Degenerative valve diseases accounted for 45.3% of patients with Valve diseases, and was seen to be the commonest diagnosis in patients aged 70 years or more which is consistent with a report from Nigeria [13].

The diagnosis of Infective Endocarditis was made using Modified Duke's criteria, among which presence of Valvular vegetation is a major criteria[29]. In our study 4.7% of patients were found to have Valvular vegetations and thus presumed to have Infective Endocarditis.

In developed countries, Mitral Valve Prolapse was reported to be the most common cause of Pathological Mitral regurgitation among patients with valve diseases [30]. Only 1.6% of our patients with Pathological MR have Mitral Valve Prolapse as etiology, which is much less compared to reports from developed countries, which could be explained with the relative abundance of alternative etiologies for valve diseases in our patients.

Patients with Prosthetic valve are quite few, despite the overwhelming magnitude of patients requiring surgical management for valve diseases. This is because of the required financial and technical input, which is not still feasible in our hospital at this point in time and these few patients are operated elsewhere with support of non-governmental organizations or individual funding. All of our patients with implanted Prosthetic valves had them for Rheumatic valvular diseases and would add up to the total load of the latter.

In our study among patients with Rheumatic Heart Diseases the mean age was 33.01±11.6 years which is higher than the mean age of patients from an earlier report in Gondar[31] likely because of exclusion of pediatric and adolescent age groups in our report, but comparable to the patient group of the former

report from Jimma[11]. We have found Multi Valve Disease which encompasses two or more Valvular involvement with rheumatic heart disease to be the commonest, Mitral Stenosis alone was found in 8 % and pure Aortic valve disease in 7 % of cases. These values vary with the report from Jimma where isolated Mitral stenosis accounted for 51.3%, combined Mitral stenosis and Mitral regurgitation for 25.4%, isolated Mitral or Aortic regurgitation each 6.2% and combined Aortic regurgitation and Mitral stenosis in 5.7%, which is possibly confounded by utilization of Echocardiography for 75.4% of the patients among the latter and the rest being diagnosed clinically [11]. While in a report by Melka A. from Gondar during the period January 94-January 95, among 114 patients with Rheumatic Heart Disease, Mitral valve disease with MR/MS was the commonest followed by MS and then MR.[31]In another report from Ghana MR was found to be the commonest.[7]

Dilated cardiomyopathy was diagnosed in 6.8% of cases, the specific etiologies of which were not specified as it is technically and financially demanding, which was as well not feasible in our setting. Compared to the reports from Ghana and Jimma occurrence was considerably less[7,11].

With the inherent limitation of echocardiography primarily in diagnosing stable Coronary artery diseases, we report 7.8% of our patients had echocardiographic evidences suggestive of ischemic heart disease, which was lower than same reports from Jimma and Ghana,[7,11]but was higher than the Nigerian group[13].

Hypertensive Heart Disease and Diastolic Dysfunction were also seen commonly. Although only 78% of patients with echocardiographic diagnosis of Hypertensive heart disease were concomitantly diagnosed as having diastolic dysfunction. The apparent failure in diagnosing diastolic dysfunction can be partially explained with the difficulty of diagnosing it in it's early and/or in the second grade using the older echocardiography machine, because of lack of tissue doppler study. The frequent occurrence of Hypertensive Heart Disease is consistent with former reports from various African countries,[7-10,13] Diastolic Dysfunction was found to be 2nd most common echocardiographic abnormality in the Nigerian study in those with age group above 50 years,[13] which is consistent with our report.

Pulmonary Hypertension was found in 32.6% of our patients. According to the revised 2008 WHO classification 69.4% had Category-2 disease[32]. Adult

congenital heart diseases were seen in 2.7% of our cases, presenting with respective decrement in occurrence from Atrial Septal defect, Pulmonary Stenosis, Bicuspid Aortic Valve, Ventricular Septal defect. The mean age of our patients with Congenital Heart diseases was 33.8±14.4 years, which shows patients presentation to health facility at a later age and mostly only when they are symptomatic, which is because of lack of awareness by the patients about heart disease and constrained cardiac care system which is not readily accessible to the public. Pericardial diseases were seen in 7.1% of the cases, 14 patients (19.2% of the later) had Constrictive pericarditis and in almost all cases Tuberculosis was considered as the likely etiology.

Few of our patients (0.4%) had echocardiographic features consistent with myocarditis, with undefined primary etiologies as we did not perform further studies to ascertain. Few patients had outlying diagnoses as Coarctation of the aorta, Patent Ductus Arteriosus, Restrictive cardiomyopathy, Cardiac masses etc.

Limitations: The study design being a single center based retrospective review of record is weak in strength to compute additional analysis and to infer associations. Echocardiographic features of Rheumatic versus Degenerative valvular heart diseases among older patients with severely calcified leaflets may be difficult. Economic state of patients was inferred indirectly from payment status of patients, which is not a standard or accurate means to assess the goal.

Conclusions: Valvular diseases remain to be the most common causes for heart diseases among adults who had echocardiographic studies in the study setting, with Rheumatic in the younger and degenerative etiologies among the elderly being predominant. We recommend population based studies to look into the magnitude of rheumatic heart disease.

#### REFERENCES

- 1. Longo D, Kasper D, Jameson J, et.al. Epidemiology of Cardiovascular disease in Harrison's principles of internal medicine. 18<sup>th</sup> ed. United States of America: McGraw-Hill companies; 2012
- 2. Anderson GF, Chu E. Expanding priorities. Confronting chronic disease in countries with low income. N EnglJMed. 2007: 356 (3): 209-211.
- 3. World Health Organization. The global burden of disease: 2004 update. Geneva: World Health Organization; 2008 [Cited Jan 2,14]. Available from: www.who.int/healthinfo/global burden disease
- 4. World Health Organization [Internet]. Deaths from non-communicable diseases on the rise, with developing world hit hardest [Updated 2011 April 27; Cited 2013 Nov.2]. Available from: www.who.int/mediacentre/news/releases/2011/ncds\_20110427/en/
- 5. Omran AR. The epidemiologic transition; a theory of the epidemiology of population change. Milbank Mem Fund Q.1971; 49:509-538.
- 6. Boutayeb A. The double burden of communicable and non-communicable diseases in developing countries. Trans R Soc Trop Med Hyg. 2006 Mar;100(3):191-9.
- 7. Amoah A.G.B. Spectrum of cardiovascular disorders in a national Referral center, Ghana. East African Medical Journal 2000: 77 (12):648-653.
- 8. Ojji DB, Alfa J, A jayi SO, et al. Pattern of heart failure in Abuja, Nigeria: an echocardiographic study. Cardiovasc J Afr. 2009: 20(6):349-352.
- 9. FreersJ, Mayanja Kizza H, Ziegler JL, et al. Echocardiographic diagnosis of heart disease in Uganda. <u>Trop Doct.</u> 1996: 26(3):125-128.
- 10. Suliman A. The state of heart disease in Sudan. Cardiovascular Journal of Africa. 2011: 22(4): 191-96.
- 11. Belete H, Fessahaye A, Dawit T. The pattern of cardiac diseases at the cardiac clinic of Jimma University specialized hospital, south west Ethiopia. Ethiop J health Sci. 2010: 20(2):99-105.
- 12. Tamirat M. Pattern of cardiac illness in children at Zewditu memorial Hospital. Ethiopian Journal of Pediatrics and Child health. 2008:4(1): 12-18.
- 13. EC Ejim, CB Ubani-Ukoma, UC Nwaneli1, BJ Onwubere. Common echocardiographic abnormalities in Nigerians of different age groups. NJCP; Jul-Sep 2013;16 (3)

- 14. Maru M. The changing pattern of cardiovascular diseases in Ethiopia. East Afr Med J. 1993 Dec;70(12):772-6.
- 15. Guteta S, Oli K, Feleke Y, Yadeta D, Mekonnen D, Tafese A. Spectrum of cardiovascular diseases among ethiopian patients At tikur anbessa specialized university teaching hospital, Addis ababa. *Ethiop med j,* 2014, vol 52, no.1
- 16. Benoy N.S. Echocardiography in the Era of Multimodality Cardiovascular Imaging. BioMed Research International. Vol. 2013 (2013), Article ID 310483
- 17. Abegaz B. Diagnostic utility of echocardiography in Ethiopia. Ethiop Med J. 1989 Jul; 27(3):129-34
- 18. J.I.G.Strang. Echoes from the third world Two-dimensional echocardiography in a developing country. S Afr Med J 1990; 77: 85-91.
- 19. World Health Organization [Internet]. Maternal, Newborn, Child and Adolescent health, Adolescent health [Cited 2013 Oct.27]. Available from: www.who.int/topics/adolescent health/en/
- 20. USAID report [Internet]. Health Care Financing Reform in Ethiopia: Improving Quality and Equity [Updated 2012 Mar.1; Cited 2013 Nov.1]. Available from: www.HealthSystems2020.org
- 21. Roberto ML, Michelle B, Richard BD, Frank AF, Elyse F, Patricia AP, Michael HP, Mary JR, James S, Jack SS, Scott DS, Kirk TS, Martin St J, William JS. Recommendations for Chamber Quantification: A Report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, Developed in Conjunction with the European Association of Echocardiography, a Branch of the European Society of Cardiology. J Am SocEchocardiogr 2005;18:1440-463
- 22. Jae K. OH et al. Valvular Heart Disease in THE ECHO MANUAL. USA. 3<sup>rd</sup> ed. Lippincott Williams & Wilkins; 2006.
- 23. World Health Organization. Rheumatic fever and Rheumatic heart disease. Report of a WHO Expert Consultation, Geneva 2004
- 24. Reményi, B. et al. World Heart Federation criteria for echocardiographic diagnosis of rheumatic heart diseasean evidence-based guideline. Nat. Rev. Cardiol.2012;9:297–309
- 25. John BC. Aortic stenosis. Eur J Echocardiogr 2009;10(1):i11 i19
- 26. Roberts WC. Morphologic features of the normal and abnormal mitral valve. Am J Cardiol.1983;51(6):1005-28
- 27. Lawrence GR, Wyman WL, Jonathan A, Lanqi H, Mark DH, Krishnaswamy C, Scott DS, Eric KL, Nelson BS. Guidelines for the Echocardiographic Assessment of the Right Heart in Adults: A Report from the American Society of Echocardiography Endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am SocEchocardiogr 2010;23:685-713
- 28. Jared WM, G. William D. Myocarditis Current Trends in Diagnosis and Treatment. Circulation. 2006;113:876
- 29. Durack DT, Lukes AS, Bright DK; Duke Endocarditis Service. New criteria for diagnosis of infective endocarditis: utilization of specific echocardiographic findings. Am J Med 1994;96:200-9.
- 30. Theal M et.al. Prevalence of mitral valve prolapse in ethnic groups. Can J Cardiol. 2004 Apr;20(5):511-5.
- 31. Melka A. Rheumatic heart disease in Gondar College of Medial Sciences Teaching Hospital: socio-demographic and clinical profile. Ethiop Med J. 1996 Oct;34(4):207-16.
- 32. Simonneau G et al. Updated Clinical Classification of Pulmonary Hypertension. JACC Volume 54, Issue 1, Supplement, 30 June 2009, Pages S43–S54

Adekunle Adesina, Abiy Hiruye, Ephrem Berhe, Amanuel Haile, Olugbenga Akinloye, Hagos Abreha, Hagazi Tesfaye, Kimberly Klaus, Fikre Enquselassie.

#### **BRIEF COMMUNICATION**

# TOWARDS A 'GLOBAL' STRATEGY FOR TACKLING THE GLOBAL BURDEN OF COMMUNICABLE AND NON-COMMUNICABLE DISEASES IN RESOURSE LIMITED SETTINGS.

Adekunle Adesina<sup>1</sup>, Abiy Hiruye<sup>2</sup>, Ephrem Berhe<sup>3</sup>, Amanuel Haile<sup>3</sup>, Olugbenga Akinloye<sup>4</sup>, Hagos Abreha<sup>3</sup>, Hagazi Tesfaye<sup>3</sup>, Kimberly Klaus<sup>5</sup>, Fikre Enquselassie<sup>6</sup>

#### **ABSTRACT**

The global burden of communicable diseases (CD) and non-communicable diseases (NCD) in low and middle-income countries (LMICs) likely stems from a common substratum of societal and system inadequacies. In order to appropriately control these conditions and to manage the determinants and deterrents of both CDs and NCDs related deaths and disabilities, joint strategies aimed at both systemic and population levels are warranted.

Although deficiencies exist within the health systems of LMICs, assets which could be leveraged efficiently to produce desirable outcomes also abound. Significant changes are already taking place through health initiatives within LMICs, opening up opportunities for further success through the involvement of international agencies. The role of these agencies, including donor countries and LMICs' Diaspora, is to strengthen and support the opportunities offered by on-going changes at the country level.

There is a need to better understand and support the drivers and processes of positive change within LMICs in order to harness them for more widespread benefit through scale-up efforts. Strategies for addressing CDs and NCDs should be devised and implemented as complementary rather than competing 'sides of the same coin'.

#### INTRODUCTION

The current status of global health is characterised by a double burden of disease due to the ongoing epidemiologic transition in low and middle income countries (LMIC), largely in Asia and Africa. Traditionally, communicable diseases (CDs) such as malaria have been the scourge of public health and clinical care for these countries. However, recognition of an increasing burden of non-communicable diseases (NCDs) is now growing: these include cardiovascular disease, cancer, diabetes and other chronic conditions. Accordingly, high-level national, regional and international initiatives are underway to tackle NCDs (1) at preventive and curative levels. These will assume greater importance and urgency as the threshold of the 2015 timeline for the Millennium Development Goals (MDGs) is crossed.

Although the increasing excess toll of diabetes and other NCD-related death and disability in LMIC is now well recognised (2), international funding resources may not be commensurate to this trend. The very nature of NCDs are such that the time delay between intervention and the onset of health benefits accruing due to disease control is less likely to sustain the interest and motivation of international donors than CDs. Given the strong focus and effort being deployed for tackling emerging Communicable Diseases such as Ebola and residual hurdles in the control of HIV/AIDs and malaria, a significant change in the funding situation in the near future is not evident. However, transferring money away from the control of CDs in order to fund the control of NCDs only amounts to 'robbing Peter to pay Paul'; this is neither a viable nor sustainable option and may have dire consequences for the overall health of LMIC populations. The danger of such an approach in global health was recently highlighted in a speech by Her Imperial Majesty the Queen in the United Kingdom and supported by expert opinion (3).

<sup>1</sup>Nuffield Department of Population Health, Linacre College University of Oxford <sup>2</sup>Ethiopian Medical Association, Addis Ababa , Ethiopia, <sup>3</sup>Mekelle University <sup>4</sup>Africare Lagos office (Head office) <sup>5</sup>Global Health Department, College of Public Health, University of South Florida, Tampa, Florida, USA <sup>6</sup>Department of Preventive Medicine, Addis Ababa University, Addis Ababa , Ethiopia

Ultimately, the dividing line between NCDs and CDs is artificial: the success of ART now means many survivors living with HIV/AIDS are at risk of the residual NCD-type effects of previous damage to organ systems such as kidney and bone-marrow resulting from the disease as well as ART use. Also it has been shown that the rising cardiovascular burden in LMIC due to ischaemic heart disease is occurring against the backdrop of a far greater burden of CDs-related valvular heart disease (4), the majority of which is rheumatic.

Tackling the current scenario clearly calls for fresh, 'outside-the-box' thinking in terms of research, policy and practice. This must take into consideration not only disease control per se, but also the systems and structures in place for improving chronic health and well-being. Such structures must aim to increase the sense of ownership over their own health among populations in LMIC, including awareness of potential NCD conditions and a willingness to take part in prevention efforts. This paper attempts to describe the global strategies for tackling the global burden of commnicable and non-communicable diseases in resource limited settings.

#### METHODS AND MATERIALS

Over the past decade there have been a myriad of widely publicised initiatives for global health concerns other than NCDs among governmental, intergovernmental and non-governmental organisations (NGOs) (1). Back in April 2013, members of The Health Network for Health and Development met with researchers and policy makers in Copenhagen to deliberate on new approaches which aim at synergies rather than competition between strategies for the control of NCDs and CDs in LMIC. A broad range of strategies were addressed, including work force development, rights-based approaches, community ownership and individual responsibility, and how to "break the silos of NCDs and CDs". The main thrust of the deliberations was "bridge building" between NCDs and CDs, starting with prevention and carrying through treatment and into rehabilitative care.

During five series of annual symposia at the University of Swansea, organised by Health Works International Support Systems (HISS) from 2006 through to 2010, we proposed a shift in the international health paradigm of aid and assistance to one of enhancing health in disadvantaged regions through systematic

sourcing, sharing, and sustaining of success stories in health care initiatives emanating from those same regions. Building on the work of HISS, we undertook an exploratory ethnographic effort focused on the physical state of communities, human interactions, and their activities and voiced aspirations. We then worked through health care settings, schools, social milieu and events such as churches and cultural celebrations over a two-month period, culminating in a street campaign that promoted renal and general health awareness. The campaign, which targeted both CDs and NCDs, focused on the behavioural risks for both high blood pressure and poor hand hygiene. Demonstrations and displays highlighted safe dietary practices (reducing salt intake) as well as methods by which personal and hand hygiene can be maintained.

#### RESULTS

Overall, we found both significant untapped opportunities for learning within the health care system and the community and also key psychological and social obstacles to the attainment of renal and general health. Ordinary and uneducated members of the community were very willing to acquire new knowledge and skills about disease control and to participate in the process of health improvement. However, we also noted inaccurate perceptions of the cost of personal preventive primary health care, even among the educated members of the community. A short questionnaire on risk factors and awareness of renal and related health conditions identified these concerns among 5-11% of 213 participants from the streets and health centres. In the two-month campaign, we were also able to create crucial connections between the Health Service in Northern Ethiopia and their descendants in the Diaspora who have expertise in health care.

GHANA: Electronic Health Records: In Ghana, electronic health records have been implemented using a system that was rigorously tested at Korle Bu University Teaching Hospital. The WHO supported project provides customised software that allows for real time collection of health information. The Ghanaian Health Ministry recognizes that electronic health records hold promise for the improvement of health care improvement and avoidance of waste (5).

NIGERIA: National Health Bill 2014 and Epidemic Control:

After its tempestuous ten-year passage through the Nigerian legislative processes, a National Health Bill was passed in 2014. The newly defined roles and responsibilities and funding offered with robust governance requirements offer hope of lifting the delivery of primary health care out of dependence on Nigerian politics. An exemplary effort to contain the Ebola epidemic has also been widely hailed as a success story, as has continuing success in the control of residual endemic polio through the work of the Nigeria Primary Health Care Development Agency (NPHCDA) (6).

ETHIOPIA: Health Extension Workers: At this time last year Ethiopia was recognised by UNICEF to have achieved a marked reduction in child mortality to MDG targets through the deployment of Health Extension workers for the delivery of basic health care (7). The success of this program was also widely celebrated in the British lay press as well as in the House of Lords (8).

Mobile Technology for Health: In Ghana, Nigeria, Ethiopia, and Kenya, the emergence and growth of modern electronic technologies also provides hope for innovative opportunities to improve population health. These technologies may distribute educational messages in health promotion campaigns, aid in monitoring and managing disease, and assist in the provision of rehabilitative car.

#### DISCUSSION

Perhaps the need for innovative strategies has been most well captured in the work of Lord Nigel Crisp. In his extensive ground level consultations in LMIC, particularly sub-Saharan Africa, he identified a significant desire to take more ownership in the process of health care delivery amongst ordinary persons in local communities. He also recognized opportunities for researchers and health care workers to not only teach, but also to learn from these individuals. He continues to campaign for this novel mutual learning approach as a basis for international partnerships in improving global health (9), and recent developments in the attitudes, approaches and actions of opinion leaders in Africa have advocated similar ideas.

At the 58<sup>th</sup> Health Ministers Conference (HMC) for East, Central and Southern Africa (ECSA), which included Health Ministers and senior executives from 11 countries (1-4) and several global health thinktanks, Omaswa, the founding Executive Director of

the Global Health Workforce Alliance noted a "fresh move in the right direction." He highlighted "the capacity and synergies of local institutions being strengthened, and the Health Ministers Conference embracing the relevance and importance of building stewardship and leadership capacities of the Ministers themselves and of their Ministries to support them". He further opined that "transformative and sustainable change is endogenous" and "that capacities of the institutions and individuals should built from what is already available" (10).

It is important that health systems be designed and delivered in line with humanitarian principles, but it should not be delivered solely as an emergent humanitarian response, as this may undermine long-term benefits. The health community must take advantage of existing assets to strengthen systems within LMICs and also seek new opportunities so that improved outcomes can be sustained; intersectoral leverages can contribute if necessary.

Overall, significant changes are already taking place through health initiatives within LMICs, opening up opportunities for further success through the involvement of international agencies. Clearly, maximizing the promise and full potential of these opportunities will require political power and support from leaders in LMICs. Attempts to capitalize on existing potential will also benefit from the collaboration of the international community, donors and Diaspora alike. These supporters can act as catalysts who help create and consolidate collective health consciousness and responsibility in communities and the political class in LMICs (11).

Considering the prevention and treatment of NCDs and CDs as synergistic rather than alternative strategies, rewarding demonstrable political will, and stimulating home-grown policy initiatives will all be crucial in successful implementation in the future. The role of the research community is to discover and highlight emerging examples of successful home -grown initiatives. Key questions that must be addressed about these programs include: "Why is this happening now? Why is this happening here (and not in other health sectors or other countries in the region)? How can inter-sectoral collaborative resources be used to further enhance positive changes and enable the systems to sustain them? How can the changes be supported, scaled up and sustained with input from international donors and the Diaspora?"

Raising and answering these questions may be one vital component of efforts to provide sustainable

improvements in health in Africa and other LMICs. It can also serve as a springboard for future efforts in international health and development. In conclusion, we urge the international health care community to envision health care plans for CDs and NCDs as synergistic rather than as competing priorities.

We call for a fresh focus on strengthening health systems and *outcomes* and offer renewed enthusiasm to proactively seek out existing *opportunities* to improve them, even in the under-resourced scenario of African and LMICs.

#### REFERENCES

- 1.. Thomas J Bollyky EJE, Eric P Goosby,, David Satcher DES, Tommy G Thompson. NCDs and an outcome-based approach to global health. Lancet. 2014;384(Issue 9959):2003-4.
- 2. Federation ID. IDF Diabetes Atlas 2014 [Six edition]. 1-2]. Available from: http://www.idf.org/sites/default/files/Atlas-poster-2014\_EN.pdf.
- 3. Guardian T. Queen fears 'malaria comeback' [News Paper]. [updated 18 November 2014]. <a href="http://www.telegraph.co.uk/news/uknews/theroyalfamily/11239497/Queen-fears-malaria-comeback.html">http://www.telegraph.co.uk/news/uknews/theroyalfamily/11239497/Queen-fears-malaria-comeback.html</a>.
- 4. Senbeta Guteta Abdissa KO, Yeweyenhareg Feleke Gebreyes, Dejuma Yadeta Goshu, Dufera Mekonnen Begna, Abinet Tafese. Spectrum of cardiovascular diseases among Ethiopian Patients at Tikur Anbessa University Teaching Hospital, Addis Ababa Ethiopian Medical Journal. 2014;52(1):9-17.
- 5. Ghana adopts electronic health records 2014 [cited 36 3]. 12]. Available from: http://africa-health.com/articles/march 2014/News.pdf.
- 6. AN ACT TO PROVIDE A FRAMEWORK FOR THE REGULATION, DEVELOPMENT AND MANAGEMENT OF A NATIONAL HEALTH SYSTEM AND SET STANDARDS FOR RENDERING HEALTH SERVICES IN THE FEDERATION, AND OTHER MATIERS CONNECTED THEREWITH, 2014., SB. 215 (2014).
- 7. Crowe S. In Ethiopia, a far-reaching health worker programme has helped reduce child mortality across the country. Available from: http://www.unicef.org/infobycountry/ethiopia\_70372.html.
- 8. Strengthening Health Systems in Developing Countries International Development Committee:http://www.publications.parliament.uk/pa/cm201415/cmselect/cmintdev/246/24607.htm.
- 9. Bristol N. Lunch with The Lancet [m]. 2010 [updated 13 March; cited 375 9718]. 885]. Available from: http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(10)60375-3/fulltext.
- 10. Omaswa F. 'Inclusive Africa' is the way forward 2014 [cited 36 3]. 7]. Available from: <a href="http://www.africa-health.com/articles/march\_2014/Omaswa.pdf">http://www.africa-health.com/articles/march\_2014/Omaswa.pdf</a>.
- 11. Gwata D. BMA, Free for all Blog [Internet]: BMA. 2015. [cited 2015 6 January 2015]. Available from: https://communities.bma.org.uk/bmaspace/b/weblog/archive/2015/01/02/compassion-without-borders-notes-from-an-ebola-frontline.

#### **Brief Communication**

# ACUTE APPENDICITIS IN CHILDREN ADMITTED TO ZEWDITU MEMORIAL HOSPITAL

Zelalem Assefa, MD<sup>1</sup>, Awetash G/yesuse, MD, MPH<sup>2</sup>

# **ABSTRACT**

**Background**: Acute appendicitis is the most common cause of acute abdomen in children. The rate of appendicular perforation may be related to duration from the onset of symptom presentation to treatment.

**Objective**: To describe the clinical characteristics and assess symptom duration as a risk factor for perforation in children with acute appendicitis.

**Patents and methods**: A retrospective analysis of medical records of 322 children under 15 years of ages with intraoperative diagnosis of acute appendicitis between the periods of September 2006 and August 2010.

Results: Acute appendicitis accounted for 87.5% of all cases of acute abdomen during the study period. Two hundred patients were boys and 122 patients were girls giving male to female ratio of 1.6:1. The mean and median ages were 10.4 and 11 years respectively. The youngest patient was 3 years old. The peak age range was 10-14 years. The most common presenting symptoms were abdominal pain (100%), anorexia (85.1%), vomiting (83.9%), and fever (82.3%). Right lower quadrant tenderness was the leading physical finding observed in 83.9% of patients. The mean duration of symptoms in children with non-perforated appendicitis was 2.5 days whereas the mean duration of symptoms in children with perforated appendicitis was 5.2 days. The mean length of hospital stay in children with non-perforated appendicitis was 3.6 days whereas the mean length of hospital stay in children with perforated appendicitis was 8.4 days. Leucocytosis was observed in 74.5% of children and the mean leucocyte count was 13150/mm³. The incidences of perforation if symptoms were present for less than 24 hours,24-48 hours and more than 48 hours were 4.1%, 10.2%, and 45.3%, respectively. Postoperative wound infection was observed in 1.9% and 31% of children with non-perforated and perforated appendicitis, respectively. Two children died in the hospital.

**Conclusion**: Acute appendicitis was the commonest cause of acute abdomen in children. It was more prevalent in children aged 10-14 years. The commonest presenting symptoms and signs were abdominal pain, anorexia, vomiting, and fever and right lower quadrant tenderness. The risk of perforation is directly proportional to the duration of illness at presentation. Perforated appendicitis was associated with increased morbidity, mortality and prolonged hospital stay.

**Keyword**: appendicitis, clinical characteristics, symptom duration, appendicular perforation

#### INTRODUCTION

Acute appendicitis refers to acute transmural inflammation of the vermiform appendix. It is the most common acute surgical condition in children (1-3). In the USA, the incidence of acute appendicitis increases from an annual rate of 1-2 per 10000 children between birth and 4 years of age to 19-28 per 10000 children younger than 14 years (4, 5). Acute appendicitis was very rare in African populations but it is now thought to have increased in incidence. This is

believed to be due to the adoption of more western patterns of life(6). In some parts of the African continent, it has become one of the commonest surgical emergencies(7,8). Appendicitis could occur in all age groups but its incidence peaks in the second decade of life and rarely occurs in infants. It affects males more often than females (1,4,9,10).

Appendicitis in children has broad spectrum of clinical presentation depending on the timing of presentation, the patient's age, the position of the appendix, and individual variability in the evolution of the disease process. Because of the multitude spectra of

<sup>&</sup>lt;sup>1</sup>Department of Surgery, Addis Ababa University- College of Health Sciences

<sup>&</sup>lt;sup>2</sup>Asefa Gobezie Memorial Melbourn Hospital

clinical presentation, it may be difficult to distinguish appendicitis from other causes of abdominal pain. Whereas the classic presentation of acute appendicitis is well described, this represents less than half the cases(1,9,10). A child with acute appendicitis may present with abdominal pain, vomiting and diarrhea, whereas the clinician, due to the commonness of the disease, may entertain acute gastroenteritis as the first impression which would lead to misdiagnosis, inappropriate treatment and complications. A primary focus in the management of acute appendicitis is avoidance of sepsis and the infectious complications seen in association with perforation. Appendicular perforation is a major problem in children. Various factors have been mentioned to be associated with appendicular perforation and complication. Delay in diagnosis was reported as a risk factor for perforation in studies by Michael B., et al(11) and Abantanga FA(12). Parental delay was observed as a major risk factor in a study by Eldar et al (13). The objectives of this study, therefore, were to describe the clinical characteristics and assess the relationship between duration of symptoms with appendicular perforation at Zewditu hospital, and to compare results with other studies.

# PATIENTS AND METHODS

This is a retrospective analysis of children under 15 years of ages who were operated up on for acute appendicitis at Zewditu Memorial Hospital (ZMH) in Addis Ababa, Ethiopia. The hospital is a referral hospital that delivers surgical services to elective and emergency patients coming from the city and neighbouring villages. It is also a teaching hospital that provides surgical education to medical students and surgical residents.

All medical records of children under 15 years of age who were operated for acute appendicitis at ZMH between September 2006 and August 2010 were reviewed. Children with intraoperative diagnosis of acute appendicitis were considered eligible for the study. Variables were extracted on a prepared format and data were descriptively analysed using EPI-INFO version 6.04 statistical software with Chisquare test. A P-value <0.05 was taken as a level of significance and results were presented in percentage and tables.

#### **RESULTS**

A total of 416 children were operated up on for acute abdomen during the study period. Out of these ,375 children were operated up on for a clinical diagnosis of acute appendicitis. Out of the 375 children, 11 (6boys and 5 girls) had negative appendectomy for grossly normal looking appendices whereas acute appendicitis was entertained in the remaining 364 children. Out of the 364 children with intraoperative diagnosis of acute appendicitis, medical records of 322 children were possible to retrieve for inclusion in this study.

Out of the 322 patients,200 were boys and 122 were girls giving male to female ratio of 1.6:1. Two hundred ninety three children (91%) were from Addis Ababa and 29(9%) were from outside Addis Ababa. The mean age was 10.4±2.1 years and 11 years was the median age. The youngest child was 3 years old. The peak age range was 10-14 years. The age and sex distribution of patients is shown on Table 1.

Table 1: Demographic characteristics in 322 children operated for acute appendicitis, ZMH, September 2006-August 2010

| Character | ristics             | Frequency         | Percentage |
|-----------|---------------------|-------------------|------------|
|           |                     |                   |            |
| Age 0     | )-4                 | 2                 | 0.6        |
|           | 5-9                 | 111               | 34.5       |
| 1         | 10-14               | 209               | 64.9       |
| Mean age  |                     | 10.4 <u>+</u> 2.1 |            |
| Median    |                     | 11                |            |
| Ra        | ange                | 3-14              |            |
| G         |                     | 104               | (0.2       |
| Sex       | M                   | 194               | 60.2       |
|           | F                   | 128               | 39.8       |
| Resident  | Addis Ababa         | 293               | 91.1       |
|           | Outside Addis Ababa | 29                | 9.0        |
|           | Outside Addis Ababa | 29                | 9.0        |

Symptoms and signs of presentation to the hospital are shown on Table2. All patients had abdominal pain and migration of pain to the right lower quadrant was observed in 64.9% of children. Anorexia and vomiting were the next common presenting symptoms. Right lower quadrant (RLQ) tenderness was the leading physical finding observed in 83.9% of patients. The duration of symptoms before presentation ranges from 12 hours to 5 days with the average duration being 2.5±1.3 days with a median duration of 3 days in children with simple appendicitis; whereas the duration of illness at presentation in children with perforated appendicitis ranges from 24 hours to 15 days with the average duration being 5.2±1.7 days with a median duration of 5.5 days (p<0.03). The average length of hospital stay in children with simple appendicitis was 3.6±1.4 days, median 4 days with a range of 2-6 days whereas the average length of hospital stay in children with perforated appendicitis was 8.4±2.3 days, median 8.5 days with a range of 6-25 days(p<0.01).

Symptoms and signs of presentation to the hospital are shown on Table2. All patients had abdominal pain and migration of pain to the right lower quadrant was observed in 64.9% of children. Anorexia and vomiting were the next common presenting symptoms. Right lower quadrant (RLQ) tenderness was the leading physical finding observed in 83.9% of patients. The duration of symptoms before presentation ranges from 12 hours to 5 days with the average duration being 2.5±1.3 days with a median duration of 3 days in children with simple appendicitis; whereas the duration of illness at presentation in children with perforated appendicitis ranges from 24 hours to 15 days with the average duration being 5.2±1.7 days with a median duration of 5.5 days (p<0.03). The average length of hospital stay in children with simple appendicitis was 3.6±1.4 days, median 4 days with a range of 2-6 days whereas the average length of hospital stay in children with perforated appendicitis was 8.4±2.3 days, median 8.5 days with a range of 6-25 days(p<0.01).

Table 2: Clinical presentation in 322 children operated for acute appendicitis, ZMH, September 2006-August 2010

| Clinical presentation* | No of Patients (%) |  |
|------------------------|--------------------|--|
| Symptoms               |                    |  |
| Abdominal pain         | 322(100)           |  |
| Anorexia               | 274(85.1)          |  |
| Vomiting               | 270(83.9)          |  |
| Fever                  | 265(82.3)          |  |
| Pain shift to the RLQ  | 209(64.9)          |  |
| Constipation           | 59(18.3)           |  |
| Diarrhoea              | 49(15.2)           |  |
| Signs                  |                    |  |
| RLQ direct tenderness  | 270(83.9)          |  |
| Rebound tenderness     | 189(58.7)          |  |
| Generalised tenderness | 52(16.1)           |  |
| RLQ mass               | 11(3.4)            |  |

<sup>\*</sup>N.B. multiple symptoms and signs are possible

Duration of illness at presentation in children with

- Non perforated appendicitis: Mean 2.5±1.3 days (Range 12 hours -5 days)
- Perforated appendicitis: Mean 5.2±1.7 days (Range 24 hours-15 days)

Hospital stay in children with

- Non perforated appendicitis: Mean 3.6±1.4 days (Range 2-6 days)
- -Perforated appendicitis: Mean 8.4±2.3 days (Range 6-25 days)

Table 3 shows the leucocyte count of the patients. Leucocytosis (WBC count >10000/mm³) was found in 74.5% of the patients and neutrophila (neutrophil count percentage >75) was observed in 71.1% of children. The mean leucocyte count was 13150/mm³ with a range 2890-44420/mm³.

The intraoperative gross pathologic findings were shown on Table 4. Simple appendicitis was found in 32.3% of patients and appendicular perforation was observed in 59.6% of children. The incidences of perforation if symptoms were present for less than 24 hours, 24-48 hours and more than 48 hours were 4.1%, 10.2% and 45.3 %( p<0.001), respectively.

Table 3: White blood cell (WBC) count in 322 children operated for acute Appendicitis ,ZMH, September 2006-August 2010.

| WBC count(/mm³) | No of patients (%) |  |
|-----------------|--------------------|--|
| 2890-10000      | 82(25.5)           |  |
| 10001-20000     | 209(64.9)          |  |
| 20001-30000     | 20(6.2)            |  |
| >30000          | 11(3.4)            |  |
| Neutrophils (%) |                    |  |
| >75             | 229(71.1)          |  |
| ≤75             | 93(28.9)           |  |
|                 |                    |  |

| Table 4: Intraoperative gross pathologic findings in 322 children operated for acute appendicitis, ZMH, September |
|---|
| 2006-August 2010  |

| Gross pathology         | No of patients (%) |   |
|-------------------------|--------------------|---|
| Simple appendicitis     | 104(32.3)          | _ |
| Gangrenous appendicitis | 6(1.9)             |   |
| Perforated appendicitis | 192(59.6)          |   |
| Appendiceal abscess     | 20(6.2)            |   |
| Total                   | 322(100)           |   |

Postoperative wound infection was observed in 1.9% and 31% of children with non-perforated and perforated appendicitis, respectively (p<0.001). Two children (0.62%) died postoperatively. Both were eight years old female children who came after a week from the onset of their illness and had perforated appendicitis with generalised peritonitis.

#### **DISCUSSION**

Acute appendicitis is the most common acute surgical condition in children and a major cause of childhood morbidity (1-3). In our study acute appendicitis accounted for 87.5% of acute abdominal emergencies in children .Acute appendicitis accounted for 62.3% of all abdominal emergencies in children in a study conducted in Bangui, Central African Republic (14). The negative appendectomy rate in this study was 2.9%. Negative appendectomy rate of 5% was observed in a study by Kosloske AM, et al(15). Negative appendectomy rates of 14%(16), 15%(17) and 17%(18) were reported in other studies. The low rate of negative appendectomy that was observed in this study may be because the diagnosis of appendicitis in our set up was based on a subjective perception of macroscopically abnormal appendix rather than more objective microscopic findings. Even if no apparent explanation could be given ,the male to female ratio was 1.6:1 in this study and higher incidences of acute appendicitis were also observed in males in other studies with a male to female ratio of 1.3:1(19), 1.4:1(4,20), 1.5:1(21), 1.7:1(22), and 2.2:1 (12). We observed that the mean age of children with acute appendicitis was 10.4±2.1 years. A mean age of 10.1±2.8 years(12), 9.6 years(15), 10 years(19), 12 years(20), and 9.3 years(22) were reported in other studies. The median age in our study was 11 years and this was shown to be 8 years in Abebe's et al study (22). The highest incidence of acute appendicitis was observed in age group between 10-14 years in this study and this was shown to be between 10-12 years in the study by Orvar J et a l(21). Abebe B., et al, however, showed 5-10 years of age to be the peak incidence of acute appendicitis (22). The youngest child in this series was 3 years old and the same was observed in a Nigerian study (23). The youngest age in Kosloske's, et al (15) and Abebe's, et al (22) reports was 1 year. Four years of age was the youngest child in Willmore's, et al report (16). Six months of age, however, was the youngest age in the study by Pearl RH et al (20).

Absence of cases of acute appendicitis in children under 3 years of age in our series may be due to misdiagnosis. The commonest presenting symptoms and signs in this study were abdominal pain, anorexia, vomiting, fever and RLQ tenderness which were observed in 100%,85.1%,83.9%,82.3% and 83.9% of the patients, respectively. Abdominal pain (98%), fever (86%), vomiting (82%), and RLQ tenderness (90%) were the commonest symptoms and signs observed in Orvar J, et al study (21). The commonest presenting symptoms and signs observed by Abebe B., et al were abdominal pain (99.3%), fever(91.2%), vomiting(90.5%) and direct abdominal tenderness(98%). Anorexia was observed in only 10.2% of the cases which is far lower than from our finding(22). Diarrhea was observed in 15.2% of children in this series and 11.6% was the observation made by Abebe et al (22).

Diarrhea was found in 7.6% of adult patients in a study by Abraham D., et al(24). This shows that diarrhea as symptom of acute appendicitis may be seen more in children than in adults. The study showed that the mean durations of symptoms before presentation in children with non-perforated and perforated appendicitis were 2.5±1.3 and 5.2±1.7 days respectively and this shows that delayed presentation was significantly associated with appendicular perforation which is in agreement with other

studies (12,13,22,25). In this study the median length of hospital stay in children with non-perforated appendicitis was 3.5 days whereas the median length of hospital stay in children with perforated appendicitis was 8.5 days indicating a significant association between appendicular perforation and prolonged hospital stay which is in agreement with observations by Abebe B., et al (22), Narsule CK, et al(25),Nance ML,et al(26)) and Esposito C, et al (27). The prolonged hospital stay observed may be due to the associated morbidities following appendicular perforation.

Leucocytosis with neutrophil predominance was observed in the majority of our patients and this was in line with other studies (21,22,26,28,29) but Adekunle O.O., et al from Nigeria observed leucocytosis in only 48% of their patients which is far lower than our finding (23). Appendicular perforation was found in 59.6% of patients in this study and comparable perforation rates were reported in other studies (21,22,30,31). When compared to this study, apparently lower rates of perforations were reported in studies by Michael B., et al(37%)(11), Eldar S., et al, (32%)(13), Willmore W.S., et al (22%)(16) and Birhanu K., et al (41%)(32). The higher rates of perforation that was observed in this series was the result of delayed presentation.

The wound infection rate in children with perforated appendicitis was 31% and this was shown to be 27.6% in a study by Orvar J et al (21). When compared to the wound infection rate in non perforatedappendicitis(1.9%), perforative complication is associated with higher rate of wound infection. A mortality rate of 0.62% was observed in this study. Mortality rates of 0 %( 20, 33, 34),1.0%(12), 2.7% (21), 0.68%(22), and 0.4 % (35) were reported in other studies. The mortality rate observed in this study, even if comparable to or even better than from some other African studies, may be significant when compared to the 0% mortality from the developed world and this may be due to better awareness of the disease and better health care facilities in the Westerners.

In conclusion: Acute appendicitis was the commonest cause of acute abdominal emergency in children in ZMH. It was more prevalent in children aged 10-14 years .The commonest symptoms and signs of presentation were abdominal pain, anorexia, vomiting, fever and RLQ tenderness. The risk of perforation was directly proportional to the duration of illness at presentation. Perforated appendicitis was associated with increased morbidity, mortality and prolonged hospital stay. Lack of parental awareness about the disease and misdiagnosis at prehospital levels may be reasons for late presentation. Further prospective study is recommended .

# **REFERENCES**

- 1. John J. Aiken, Keith T. Old. Acute appendicitis. In: Robert M. Kliegman, Bonita F. Stanton, JosephW. St. Geme, III, Nina F. Schor, Richard E. Behrman. Nelson Textbook of Pediatrics,19<sup>th</sup> edition. Saunders Company 2011: 1349-1355
- 2. Scholer SJ, Pituch K, Orr DP, Dittus RS. Clinical outcomes of children with acute abdominal pain. Pediatrics 1996; 98:680
- 3. Reynolds SL, Jaffe DM. Diagnosing abdominal pain in a pediatric emergency department. PediatrEmerg Care 1992; 8:126
- 4. Addis DG, ShafferN, Fowler Bs, Tauxe RV. The epidemiology of appendicitis and appendectomy in the United States. Am J Epidemiol 1990; 132:910.
- 5. OhmannC,FrankeC,KraemerM,Yang Q.[Status report on epidemiology of acute appendicitis]. Chirurg 2002; 73:769
- 6. Anonymous. Appendicitis(editorial). East Afr. Med. J. 1990: 67; 597-598
- 7. Ajao. O.G. Appendicitis in a Tropical African Population. J Nati. Med. Ass. 979; 71:997-999
- 8. Fulton, J. and Lazarus, C. Acute appendicitis among black South Africans, S. Afr. J. Surg. 1995; 33: 165-166
- 9. John Maa, Kimberly S.Kirkwood. The appendix. In:Courtney M. Townsend, R.Daniel Beauchamp, B. Mark Evers, Kenneth L. Mattox. Sabiston Textbook of Surgery. The Biological Basis of Modern Surgical Practice, 18<sup>th</sup> edition. Saunders Company 2008: 1333-1345
- Bernard M. Jaffe, David H. Berger. The appendix. In: F.CharlesBrunicardi, Dana K. Anderson, Timothy R. Billiar, David L.Dunn, John G. Hunter, Jeffrey B. Matthews, Raphael E. Pollock. Schwartz's Principles of Surgery, 9<sup>th</sup> edition. The McGraw-Hill Companies, Inc. 2010:1073-1089

- 11. Michael B. and David L. Perforated appendicitis: Current experience in a children's hospital. Ann. Surg. 1977;185:84-8732.
- 12. Abantanga FA. Acute Appendicitis in children in Kumasi, Ghana: Macroscopic Findings at Laparotomy. African Journal of Paediatric Surgery Vol 1,2004: 6-10
- 13. Eldar S., et al. Delay of surgery in acute appendicitis. Amer. J. surg. 1976;131:533-535
- 14. BobossiSerengbe, G., et al. Acute abdominal pain in children at the Pediatric Hospital in Bangui. Epidemiological, clinical, therapeutic and evolutive aspects. 2002, Arch. Pediatr., 9:136-141
- 15. Kosloske AM, Love CL, Rohrer JE, Goldthorn JF, Lacey SR. The diagnosis of appendicitis in children: outcomes of a strategy based on pediatric surgical evaluation. Pediatrics. 2004 Jan; 113:29-34
- 16. Willmore W.S., Hill A.G. Acute Appendicitis in a Kenyan Rural Hospital. East Afr. Med. Journal Vol 78:7.July 2001
- 17. Flum DR, Koepsell T. The clinical and economic correlates of misdiagnosed appendicitis: nationwide analysis. Arch Surg. 2002; 137: 799-804
- 18. Chamisa I. A clinicopathological review of 324 appendices removed for acute appendicitis in Durban, South Africa. Ann R Coll Surg Engl. 2009 November; 91(8): 688-692
- Geryk B, Kubikova E. The clinical picture of acute appendicitis in children. Rozhl Chir. 1998 Apr;77(4):142-
- 20. Pearl RH, Hale DA, Molloy M, Schutt DC, Jaques DP. Pediatric appendectomy. J Pediatr Surg 1995 Feb;30 (2): 173-8
- 21. Orvar J, Mesfin A, Adem A, Demissie H. Appendicitis in childhood. Ethiop Med J 1981; 19; 1-79.
- 22. Abebe B., Amha M. Clinical profile and risk factors for perforation of acute appendicitis in children. East Afr. Med. J. 2006;83:434-438
- 23. Adekunle O.O. and Funmilayo J.A. Acute appendicitis in Nigeria. J.Roy. Coll. Surg. Edin 1986; 31:102-104
- 24. Abraham D., Birhanu T. Pattern and Clinical Presentation of Acute appendicitis in Adults in Zewditu Memorial Hospital. Ethiop J. Health Sci. July 2003;Vol 13(2):117-123
- 25. Narsule CK, Kahle EJ, Kim DS, Anders on AC, Luks FI. Effect of delay in presentation on rate of perforation in children with appendicitis. Am J Emerg Med.2011 Oct; 29(8):890-3
- 26. Nance ML,AdamsonWT,Hedrick HL. Appendicitis in the young child: a continuing diagnostic challenge. PediatrEmerg Care 2000 Jun;16(3):160-2
- 27. Esposito C, Borzi P, Valla JS, Mekki M, Nouri A, Becmeur F, Allal H, Settimi A, Shier F, Sabin MG, Mas troianniL. Laparoscopic versus open appendectomy in children: a retrospective comparative study of 2332 cases. World J Surg. 2007 Apr;31(4):750-5 28. Lee C.M. and Teoh M.K. Perforated appendicitis: The Malaysian experience: J. R. Coll. Surg. Edin. 1990; 35:83-87
- 29. Raftery A.T. The value of the leukocyte count in the diagnosis of acute appendicitis. Brit. J. Surg. 1976; 63:143-144
- 30. Zelalem A. Acute appendicitis in Yirgalem Hospital, Southern Ethiopia. Ethiopia Med. J. 2002;40:155-162
- 31. Ephrem D. and Desalegn M. Childhood appendicitis: Factors associated with its incidence and perforation in Ethiopian children. Ethiopia Med. J. 1991; 29:15-19
- 32. Birhanu K. and Gashaw M. Acute appendicitis in Ethiopia. East Afr. Med. J. 1996: 73: 251-252
- 33. Holgersen LO, Stanley-Brown EG. Acute appendicitis with perforation. Amer. J. Dis. Child. 1971; 122:288
- 34. Marchildon MB, Dudgeon DL. Perforated appendicitis: Current experience in a children's hospital. Ann Surg 1977; 185: 84-7
- 35. Moore SW, Schneider J. Acute appendicitis in childhood: Experience in a developing country. Pediatr Surg Int 1995;10: 71-5.

#### REVIEW ARTICLE

# ABDOMINAL LYMPHOMA: IMAGING WORK UP CHALLENGES AND RECOMMENDATIONS IN RESOURCE LIMITED SETUP

Asfaw Atnafu Kebede, MD<sup>1</sup>, Frehiwot Bekele, MD, Getachew Assefa, MD<sup>1</sup>

#### **ABSTRACT**

Lymphoma management begins with an accurate diagnosis & staging. Major advances in imaging techniques, make cross sectional imaging and nuclear medicine technique an excellent tool for patient work up. However, limited access to modern imaging modality in resource limited set up and luck of standardized imaging work up challenged patient's management.

Assess the local lymphoma imaging work up and management challenges in patients with lymphoma and develop local imaging and reporting guideline.

A semistructured qualitative interview to six conveniently selected physicians (hematologists, oncologists & pathologists) who primarily takes care of lymphoma patient and literature review on the role of various imaging modalities, recommendation and experience of other countries were used as a methodology

Conventional and basic imaging modalities are used in the work up of patient in our set up. The imaging recommendation for these patients requires at least CT of the chest, abdomen and pelvis for initial diagnosis and FDG-PET and/or PET-CT for follow up and recurrence. Due to the comparable diagnostic potentials of US and its wide spread availability, makes US still the primary imaging modality. Luck of required information's and inconsistency in the radiologists report found to challenge physicians in their patient management.

The study concluded that US should still stay as the most important imaging modality in the initial treatment, staging and follow up patients in resource limited set up. It also recommended the general imaging work up and reporting framework.

Key words: Lymphoma, Ultrasound, Computed Tomography, FDG/PET, MRI

#### INTRODUCTION

Lymphoma is a general term for a group of cancers that originate in the lymphatic system and it is the most common hematopoietic malignancy. Overall incidence of lymphoma is increasing globally, with age-adjusted incidence rates for NHL being highest in developed countries. The incidence is also rising in sub-Saharan Africa where the prevalence of HIV is the highest in this part of the world (1).

Like any other disease, lymphoma appropriate management begins with an accurate and precise diagnosis; which depends on clinical, laboratory and imaging findings and criteria's. Traditionally, clinical

findings and imaging like US and CT scan was used to make diagnosis and staging which usually necessitated a surgical biopsy specimen to obtain adequate tissue(2).

Major advances in imaging techniques, during the past two decades, make cross sectional imaging an excellent tool. Imaging is not only used to suggest diagnosis but is also essential to determine the staging of disease in patients with an established diagnosis of lymphoma. Such staging is critical in determining the type, nature, and aggressiveness of treatment options to be offered to patients, as well as predicting prognosis. Where needed, imaging is also used to assess the response of lymphoma to therapy and to determine the extent of the disease when recurrence is found. Such imaging role needs multimodality

<sup>&</sup>lt;sup>1</sup>Addis Ababa University, School of Medicine, Department of Radiology

modern imaging which includes cross sectional imaging which is used to detect lymphadenopathy and the pattern of nodal involvement. Functional imaging, such as positron emission tomography (PET) using F-18-fluorodeoxyglucose (FDG), integrated with computed tomography has become widely used in the staging and evaluation of therapy response in lymphoma. It is also very useful in the follow-up of PET-avid lymphomas (2, 3).

Despite the development in imaging more than threequarters of the world's population lives in circumstances in which the possibility of receiving even the most elementary radiological services is exceedingly remote (4). In Ethiopia, like other developing countries, radiological service is poorly developed. Plain radiographs and US are the most commonly available imaging modalities. CT is available in only in few centers and MRI is just appearing in the market. Nuclear medicine service is available in only one institution in Ethiopia (5). Services like gallium-67citrate (Ga-67) scans and PET scans are farfetched at the current situation.

However, the problem is not only limited to unavailability of high tech modalities rather also lack of standardized imaging workup and reporting. Universally, the need for standardizing interpretation of imaging modalities is widely advocated so that consistent diagnosis, response assessment and follow up of patient can be made. Theoretically, any radiology report should be complete and include the structures involved, the extent of involvement, the appearance of the lesion, size and etc. The magnitude of lack of such standardized approach in our set up where basic and traditional imaging modalities employed in patient management aggravate the quality of the service rendered to patients.

Therefore, recommendation in standardizing diagnostic imaging approach and report with lymphoma promotes evidence-based practice and provides guidance to clinicians about which imaging techniques are the most appropriate in our set up to use in the workup and management of their patients. It also help the radiologist to understand the existing problem and guide them on how to make comprehensive & helpful comment for better patient management.

Thus the objectives of the review were to assess the imaging modalities used in patients with abdominal lymphoma and suggest the optimal imaging approach to be used in the local circumstances,. It also assess the challenges in reporting and attempts to develop local imaging and reporting guide line in patients with abdominal lymphoma.

# **MATERIALS AND METHODS**

Combinations of different methodological approaches were used in this study. The first method is reviewing literature on the role of various imaging modalities, recommendation and experience of other countries.

The second methodology used was conducting a semi structured qualitative interview with physicians who are involved in routine care of lymphoma patients.

In reviewing literatures: the English language evidence published on imaging abdominal lymphoma was searched through MEDLINE using the following words "lymphoma, imaging, and imaging treatment response". The pertinent literatures' identified are cross referenced to select further articles. Besides the above, no other specific search strategy was adopted. Those articles with a definitive recommendation on the imaging approaches, articles which has evidence on value of various imaging modalities are reviewed to assess the significant role of each modality. Local expert opinion was incorporated in the development of the recommendations.

A Pre-prepared format were used for the semi structured qualitative interview and done on conveniently selected two pathologists, two hematologists and two oncologists who are involved in managing lymphoma patients. The interview emphasized on their local experience on diagnosis, staging, follow up, treatment response and imaging related challenges.

# RESULTS AND DISCUSSION

Local lymphoma imaging work up & challenges: Universally hematologists, oncologists, internists and pediatricians are involved in the management of patients with lymphoma. In our set up, primary management of lymphoma patients depends on age of the patients, disease localization, disease stage, predominant site involved, type of lymphoma, patient preference, and availability of the specialty and referral preference of the primary caring doctor.

In an interview with the physicians, more than two third of the patients are primarily managed by hematologists, either pediatric or adult. The process of referral is not different from any other disease. Patients if suspected or diagnosed at different outpatient clinic are referred to the hematology team or oncology team. These clinicians are responsible for staging, treating and follow up of the patient. The oncologists, in our set up, usually take full responsibility, if disease is localized to specific organ or site or adjuvant radiotherapy is necessary. In addition, they are very much involved in managing abdominal lymphoma. Both oncologists and hematologist administer systemic anti lymphoma medication.

No joint clinic or interdepartmental management sessions specifically arranged for the management of these patients in our hospital. However, tumor board meeting with pathologists and oncologists and sometimes surgeons is done fairly regularly. It is unfortunate no radiologist is a member of this team. According to one of the oncologist lack of enthusiasm from the radiologists is the reason for not including them. The need for the presence of radiologist in the team is believed essential by all.

There are few studies done, in our set up, assessing the prevalence of lymphoma. During the interview one of the oncologist revealed that his group is reviewing fourteen years data of 13,800 patients with malignancy in oncology department. In this unpublished review, hematologic malignancy account for 1.5% of 13,800 patients of which lymphoma is the dominant (Dr. Wondimagegn, Department of Oncology/radiotherapy, AAU).

Older study done by Shamebo M et al showed that hematologic malignancies account for about 3% of hospital admissions. Among the hematological malignancies lymphoma and leukemia account for 56 % (9). According to the experience of our hematologists, approximately 5 - 9 patients/month are seen and most patients arrive late in their disease. Oncologists claim that they manage less than 2 to 3 cases of lymphoma per month. The prevalence of the disease in any given health institution depends on the level of service and availability of the specific personnel. Diagnosis is based on FNA, verification and cell marker determination done from specimen biopsy, rarely by immunohistochemistry.

According to the pathologists, Ann Arbor method of lymphoma classification is used. Once the diagnosis is proved pathologically, all patients are routinely staged, but if there are difficult or equivocal cases telemedicine technology (iPath) is used to get expert opinion. Nearly all physicians interviewed use both clinical and imaging findings (usually CXR and US)

when staging. All of them claimed that CT is rarely used in abdominal lymphoma and no MRI or any nuclear medicine techniques are used. In a review suspected 69 lymphoma patients only 9 % of these patients had CT and most of them have CXR & US (Asfaw et al. in publication process). This is in contradistinction to the routine practice elsewhere; they suggested the use of CT chest, abdomen and pelvis, PET/CT and MRI (6, 7, 8, 10, 11). Strong financial implications for routine use of CT scan & MRI and unavailability of nuclear medicine techniques forced them to entirely rely on plain radiographs and ultrasound.

In addition to the challenges of limited availability of variety of imaging modalities, the degree of information the clinicians obtained from the radiologists report is disappointing, as per the clinicians. They claimed that the reports are grossly unstandardized and the information critically wanted for staging the disease are sparsely mentioned and sometimes not mentioned at all.

As per the opinion of one of the oncologists;

"We can't even make radiotherapy planning due to the limited information from the report and the hard copy images sent with the report, which do not sometimes include the area of interest. According to his opinion, we practically have very limited assistance from imaging despite its potential".

When all the six physicians are inquired on the contribution of luck of adequate clinical information to the radiologist poor reporting? They concur with the need for information for the radiologist especially in the situation where EMR is not available. However, none of them consider it as a justification for the poor quality of radiology report.

Among the missing information from the reports, according to the physicians; poor description about the positive finding, absence of information on the extent of involvement of anatomic regions, lack of measurement of size of the pathology, deficiency of negative finding, nonexistence of recommendation on further imaging, staging, and management are included as important. They recommended the need for a standardized report and they emphasized the points mentioned above to be included. Our review could not find similar study done in developing country whether similar problem exist. However, we suppose similar problem might be seen due to the busy schedule of the limited number of radiologist.

The situation is worse in the follow up of the patients

where they claim that for practical purpose they do not use imaging. They, nearly all, claimed that they stopped relying on single reports and send patients to different private and public imaging centers so that to confirm negative or positive findings. Occasionally, they entirely rely on their clinical findings in patient follow up. They also claimed, "Absence of informative, complete and standardized report is a consistent opinion of most practicing doctors for all type of imaging and disease". This finding should be a biggest wake up call for radiologists who are involved in the examination of patients.

The physicians, claimed that the follow up of patients with lymphoma depends on the clinical condition and outcome of the patients, the extent of systemic involvement, the type of lymphoma, the regions involved and the individual clinician (specially the specialty type, oncologists in general reevaluate earlier). Imaging is also used to see the change or appearance of newer lesions during follow up.

According to, nearly all, clinicians' interviewed, the current practice where residents examining and reporting independently with limited supervision on patient's diagnostic images contribute for the incomplete and un-standardized report. They recommended the need for close supervision as a possible solution. Even though, this is not verified by the opinion of the radiologists, the authors agree that this is the current practice in the studied hospital.

The question whether to develop a standardized format, specific for lymphoma patients was positively entertained by the physicians. However, they questioned the practicality, in a situation where luck a subspecialist group of radiologist to particularly deal with these patient. They rather suggested having a format for all patients with abdominal ultrasound and specific findings like lymph node enlargement or any mass lesions or lesion in any abdominal organs to be described exhaustively irrespective of the type of disease. Most of the clinicians recommended to identify specific lesion in a particular area of the organ to be measured and this specific lesion to be measured during follow up. This is believed to be very critical in situation like ours, where EMR is not available.

# Literature review: on Imaging for diagnosis, staging and treatment response of patients with abdominal lymphoma:

Review of literature was made on the role and the recommendation of the various types of imaging used for diagnosis, staging and assessing response to therapy with abdominal lymphoma patients. Twenty one articles and peer reviewed papers and recommendations were reviewed. These articles included thirteen General review and modality based articles and eight consensus papers which suggest various recommendations and guidelines (Table).

The role of various imaging modalities in abdominal lymphoma: All reviewed literatures stated diagnostic imaging modalities to have a fundamental role in the staging of lymphomas and owing to major advances during the past two decades, make surgical staging unnecessary in most cases. Cross-sectional imaging techniques believed to be excellent tools for evaluating the extent and sites of disease in lymphomas. Despite the stated value, concern is raised in the developed countries that many imaging studies ordered during active treatment among patients with cancer for uncertain reasons and that, in some cases, results may have little or no impact on clinical care. In contrary, developing countries face challenge of luck of variety of imaging modalities.

Cross-sectional imaging (CT scan, MR imaging, US) is primarily used to detect lymphadenopathy and the pattern of nodal involvement (10, 12, 13, 14). Patients require routine follow-up to assess tumor shrinkage in response to therapy and to decide on treatment modification, if required. In most lymphoma patient's lymph node or lesion size determination before and after treatment has been suggested as a means for follow up. Measurements of lesions should be bi-dimensional. Most of these measurements are relatively easy but might be difficult in cases of irregular edges or infiltrating lesions. In some patients, lymph node attenuation values may decrease as a response to treatment with or without overall reduction in lymph node size(15-17).

The following are details, according to the reviewed literatures, illustrating the roles & limitation of various imaging modalities in imaging lymphoma.

Computed tomography: Most western literatures suggested clinical management of lymphoma to be decided based on either contrast enhanced CT or PET. CT scan is the most commonly used imaging modality for the detection, staging, and follow-up of lymphoma. The role of CT scan in lymphoma is multifold. It is used to (1) define the full extent of disease to allow accurate staging; (2) assist in treatment planning (i.e., determine the site of nodal biopsy, create radiation planning portals, and select chemotherapy protocols); (3) evaluate response to therapy; and (4) monitor patient progress and possible relapse.

Contrast-enhanced computed tomography is advised in patients with abdominal lymphomas for distinguishing lymph nodes from non-opacified bowel loops and vessels, and where more precise measuring of node size is indicated. In rare cases with head and neck involvement, CECT may be useful to differentiate physiologic uptake from enlarged cervical lymph nodes(2, 6).

Various studies evaluated the use of CT, the accuracy of CT staging of abdominal lymph nodes compared with postoperative clinical stage was found to be 75%. However, poor performance of CT was described in aggressive tumors by Mikhaeel et al (11) and the reason postulated was its inability to correctly identify an early response, since it depends largely on the reduction in size of the enlarged lymphadenopathy or masses.

In a study by Zinzani et al (12) 59 patients with NHL, presenting with abdominal involvement had CT scans at diagnosis and during follow-up (median 24 months). The accuracy of CT was found to be very low, at 25%, because of the many false positives, which may be due to the CT scan inability to differentiate between active residual disease and fibrotic changes from curative therapy in patients with abdominal masses.

Moreover, other pitfall with CT is the increasing number of reports on the presence of normal sized lymph nodes with early lymphoma which affect disease staging. To overcome this pitfall comparison with the most recent CT study is suggested, however, this is often not sufficient because the growth becomes obvious only if serial studies are compared. Even then, small difference in measurement (approximately 15%) in near normal-sized lymph nodes between two CT examination is often related to "plane of section" artifact (i.e. related to slice section) and also a follow-up study in 3 months is not sufficient for follow-up of slow-growing lymphoma (2,10,11,13).

CT-based criteria of response were defined for NHL but are also often used for HL. Recommendations include separate definitions for complete remission; complete remission (unconfirmed or uncertain); partial response; stable diseases; and progressive disease. Progressive disease, for example, includes the appearance of new lesions or an increase of more than 50% in known lesions. An increase of more than 50% in the greatest diameter of any previously identified node that was greater than 1 cm also represents progressive disease (18).

MRI imaging: Comparative studies showed the accuracy of MR imaging in detecting lymph node and organ involvement is similar to that of CT. Etsoro-Tess et al studied the role of MRI in staging patients with lymphoma. They evaluated 72 previously untreated patients with chest, abdominal, and pelvic MRI. The overall sensitivity of MRI for all lymph nodes was consistent at 87%, with the majority of under staged nodes located in the para-aortic area (75%).

Overall, MRI influenced the staging (upgraded) in 11 of 74 patients (15%) and demonstrated the presence of unsuspected disease in nine of 42 patients (21%) (14). However, other multiple comparative studies showed no significant added value by the use of MRI and restricted its use whenever CNS lymphoma is suspected. Change in the signal related to fibroses and cystic change in follow up patient has been advocated by these studies. The inconsistency of the finding is the limitation of MRI as a tool to follow response to treatment except its help in assessing the nature of a residual mass detected by CT. In the future diffusion MR imaging in lymphoma patients by allowing the detection of water motion over small distances expected to add input in lymphoma management. In general, limited additional information acquired by MRI limits its wide spread use in abdominal lymphoma diagnosis and follow up (10, 14,

Ultrasound examination: Sonography is a straightforward and convenient technique to investigate lymphadenopathy. Superficial lymphadenopathy, like the region of the neck, is a common manifestation of lymphoma and detailed analysis of these glands help in suggesting the cause of the lymphnode enlargement. Most Lymphnodes in the abdomen are accessible and can be assessed transabdominally. This helps to assess which lymphnode groups are involved and assess the different US features which suggest the lymphomatous nodes. Features like size, shape, echo texture, internal architecture, presence of calcification, and color Doppler flow studies help in suggesting a lymphnode is lymphomatous or metastatic (2, 10, 17).

Sonography prove to be a useful initial investigation. However, the main disadvantages of sonography are the poor spatial resolution, its limited use in the thorax and deep retroperitoneum, and high operator dependency. Some of its limitations may be overcome by doppler sonography which offers functional imaging of the lymph node. Since feeding vessels determine tumor growth, color/power doppler sonography

(US) may be used to differentiate lymphoma from metastatic carcinoma (19). Giovagnorio and et al (20) have described that vessels could be identified in all lymph nodes in patients with lymphoma. The majority of the lymph nodes demonstrated hilar vascularity because lymphoma arises within the lymph nodes and progresses in a centrifugal fashion.

Reports suggest that intravenously administered microbubbles help the diagnosis of lymphadenopathy with accurate demonstration of vascular flow within a lymph node(21). Sonography is a noninvasive method for detecting splenic involvement in lymphoma (22). Ultrasound is also useful for the evaluation of the genitourinary tract, including possible testicular involvement. US-guided biopsies of focal lesions are useful for tissue sampling (2, 10, 13).

The studies done assessing the use of US are relatively older. Current studies done in developed nations emphasized the use of other cross sectional images like CT. No recent study, to our knowledge, recommend the use of US exclusively for staging, follow up and response assessment.

Nuclear medicine techniques: Functional imaging reflects the metabolic activity of tissues that precede anatomical changes, allowing for a more expedient change to an alternative treatment. PET with 18F-FDG can provide functional information based on the increased metabolic demands of tumor cells requiring adenosine triphosphate generated by glycolysis. In addition to detection of tumor foci in the lymph nodes and spleen, PET imaging has the ability to differentiate between aggressive and low-grade lymphomas. Aggressive lymphomas tend to have a higher 18F-FDG uptake (23). The median sensitivity and specificity reported for PET is 90.3 percent and 91.1 percent, respectively. The maximum joint sensitivity and specificity was 87.8 percent [24). Other nuclear medicine techniques like gallium 67 have been used in lymphoma; however the sensitivity and specificity of FDG PET are superior to those of gallium 67 scintigraphy in all but indolent lymphoma (18).

However, PET imaging has numerous limitations such as absence of precise anatomic landmarks for accurate localization of lesions, inherent lack of specificity (18F-FDG can be taken up by lymphomatous nodes and sites of active inflammation and physiologically by some organs) and low-grade lymphomas may not demonstrate uptake or have a low 18FDG uptake (18).

FDG PET is important in both the primary diagnosis and the evaluation of therapy in lymphoma. It is also

superior to CT&MRI in differentiation of viable tumor, necrosis, and fibrosis. Perhaps the clearest role for the use of PET in lymphoma is in post-treatment response assessment because of its ability to distinguish fibrosis or sclerosis from residual active disease. Early studies have demonstrated a role for post-therapy FDG-PET imaging in the prediction of aggressive NHL or HL recurrence (2, 10, 11, 18, 23, 25,26).

The advent of PET-CT has remarkably improved the accuracy in the diagnostic work-up of patients with lymphoma. PET-CT provides dual modality imaging, which combines the functional information provided by PET and the excellent anatomic resolution offered by CT. Despite the mentioned role of various nuclear medicine techniques their absence or their poor development status in most developing countries makes them unthinkable in these countries.

General consensus in imaging work up of lymphoma patient and adoption to local set up: Various agencies made recommendation on the use of various imaging modalities based on literature and local experience (7, 8, 10, 27 28, 29). The recommendations developed by radiology and oncology experts in Ontario are one such attempt (8). The recommendation was developed by performing detailed literature review, taking opinion of local experts and external reviewers. These expert groups recommended CT chest/abdomen/pelvic neck for staging in all patients and is generally accepted as the primary modality for suspected lymphoma and in selecting the site for surgical tissue diagnosis. For response assessment CT of at least involved area recommended, where this information alter the treatment plan. US and MRI recommended by this group to be used only in selected cases.

In following patients routine CT to be used for highrisk at presentation, after initial therapy if PET not available, those felt to be at risk of recurrence and in patients with incurable lymphoma. The role of MRI limited and used when CT is unclear, may be useful in identifying solid organ involvement. In some cases, it may show extra-nodal disease, such as bone marrow involvement when bone scan is equivocal. However US recommended to be used in few selected cases (7). A number of agencies have developed consensusbased guidelines on the use of imaging in the followup of lymphoma. FDG PET is believed to be important in both primary diagnosis and the evaluation of therapy in lymphoma. The clear role for the use of PET in lymphoma is in post-treatment response assessment because of its ability to distinguish fibrosis or sclerosis from residual active disease is widely advocated. The current hybrid PET-CT provides dual modality imaging, which combines the functional information provided by PET and the excellent anatomic resolution offered by CT is the best modality for both diagnosis and follow up. Its limited availability limits its use (28).

The American College of Radiology (ACR) publishes the ACR Appropriateness Criteria, practice guidelines with a strong consensus component. The ACR Criteria for follow-up of Hodgkin's disease strongly recommended that, for those patients with IIA sub diaphragmatic HD, chest/abdomen/pelvic CT be performed either every six months for two years, then yearly for three years, or once a year for five years, citing the potential for early curative salvage therapy (29). The Canadian Association of Radiologists recommended that, if there is clinical suspicion of relapse or progression, a chest, abdomen, and pelvis CT examination would be appropriate, especially for NHL, and MRI is not indicated initially but may help to assess the nature of a residual mass detected by CT (27).

In the western world people has limited the use of US as the primary modality in lymphoma patients. Its use is limited for only initial evaluation of patients & guiding biopsies. The development of modern modalities with higher and better sensitivity and specific hindered its wide spread use. In addition sonography poor spatial resolution, its limited use in the thorax and deep retroperitoneum, and high operator dependency added impetus to its limited role.

However, US equipment and experts wide spread availability and its comparative role to CT in the abdominal imaging and the relatively large extent of information attained about the solid organs of the abdomen and other structures, US should not only be the initial imaging modality but the essential modality to be used for all patients in our set up. Its superior role in imaging superficial nodes and lesions, its role to guiding biopsies, absence of radiation especially in children, portability and the opportunity to do repeat multiple studies is an additional tip in favor of its continued use.

Therefore, it become obvious that CT and US should be the modality to be used for assessing abdominal lymphoma patients, especially at the initial diagnosis and staging. Follow up study usually done after fourth cycle of therapy, as per the local practice; also require similar examination modalities for restaging. The tendency of its increased availability and reduction in cost in our set up makes CT to be more

widely used. However use of proper technique and comprehensive and purposeful examination and standardized reporting system is essential.

The limited additional information's that can be attained by MRI in the abdomen, pelvis and its limited availability and cost restrict the routine use of this modality except in situation where CNS involvement is suspected.

#### Recommendations:

Based on the finding from the current survey and review of literature the following recommendation can be drawn in imaging management of lymphoma patients in resource limited set up;

- Abdominal US to continue to be the prime diagnostic modality in the work up of lymphoma patients and as much as possible CT scan of the chest and abdomen including the pelvis has to be included in the work up of all patients with abdominal lymphoma.
- 2. Physicians must provide adequate information on the diagnosis, treatment status and clinical stage and the purpose of the current examination and images or brief description of the previous findings to the radiologist who perform or interpret the US and CT scans. This should be emphasized until such a time where EMR is widely used.
- 3. Patients with Lymphoma must be managed as a team and as far as possible joint management session should be set up to discuss individual. specially difficult cases.
- Senior radiologist must examine/interpret and/ or report or attend the examination of these patients and guide the junior staffs report
- 5. Every abdominal US or CT report of lymphoma patient must include the following points on their report
  - Status of all solid abdominal organs, even if, findings are negative.
  - Lesions or abnormalities should be characterized in terms of size, echo appearance vascularity and precise anatomic location. In follow up study of these patients, similar description and comparative comments must be given to the requesting physicians.
  - Report must include comment on the retroperitoneal structures, the peritoneum, mesentery and

- omentum, even if found negative.
- All nodal regions has to be assessed and the regions of identified enlarged lymph nodes must be stated based on standard regional nomenclature and the uninvolved regions to be stated.
- 6. The following points must be stated on the status of identified nodes and or mass like node
  - The shortest and longest diameter of the dominant nodes
  - The dominant echo texture of most involved nodes
  - The presence or absence of calcifications, necrosis and other idiosyncrasies
  - Vascularity of the lesion based on power and color Doppler study
  - The relative relation of the involved nodes like the discreetness or matting and etc
  - Whether the node or mass like lesions relation with vascular and other abdominal organs
  - Presence of secondary effects on adjacent organs.
- With additional clinical information and imaging findings of other body regions, radiologists are commended to suggest the possible disease

- stage, cautiously.
- 8. In the follow up study comparative evaluation must be the goal and all attempt must be undertaken to do that, if not possible, the need for the comparative evaluation must be communicated in the report.
- Follow up study must state the development of new lesions and the relative condition of the previously identified lesion. In concluding the reports comment must be added the relative new status (improvement or not) and the current disease stage.
- Limitation of the specific modality should be included, if decision on a specific finding or change cannot be determined.
- 11. It is not recommended to suggest specific cell type of lymphoma, even if findings suggest so.

At last we also recommend the need for further study and interdisciplinary consensus team to be formed so that they develop national lymphoma diagnosis and management guideline.

Table: Abdominal lymphoma diagnosis, staging and follow up reviews

| Study subject area   | Focus               | Author/publication year  |
|----------------------|---------------------|--|
|                      | US                  | - Carroll BA/Semin Ultrasound , 1982   |
|                      |                     | -Tschammler A et al/ EurRadiol ,1999   |
|                      | Multimodality in-   | -Munker R etal/. Cancer 1995   |
|                      | cluding CT          | -Mikhaeel NG/ Leuk Lymphoma. 2000  |
| General review and   | -                   | -Rademaker J/ PET Clinics 2006   |
| modality based arti- |                     | - Zinzani PL et al/ Leuk Lymphoma. 2002  |
| cles                 |                     | - Masahiro/ RadioGraphics 2010; 30:939–957   |
|                      | MRI                 | - Esoro-Tess JD et al/Eur J Radiol. ,1991  |
|                      | FDG/PET             | - Schoder H et al/ I ClinOncol 2005  |
|                      | TDG/TET             | - Mikosch Pet al/ Acta Med Austriaca 2003  |
|                      | General review      | - Mattew J et al/ ClinOncol 1989   |
|                      | Ocheral review      | - Munazza A et al/ RadiolClin N Am 46 (2008)   |
|                      |                     | - Rankin SC et al/ Eur J Nucl Med Mol Imaging 2003   |
| Concensus nones      | Diagnosis & staging | - Lister TA et al / ClinOncol 1989   |
| Consensus paper      | Diagnosis & staging |  |
|                      |                     | <ul> <li>Cancer action Ontario/ Recommendation report 2008</li> <li>Canadian Association of Radiologists/2005</li> </ul> |
|                      |                     |  |
|                      |                     | - ACR appropriateness criteria /2000   |
|                      | Post therapy follow | -Cheson BD et al/ J ClinOncol 2007   |
|                      | up                  | -Expert Panel on Radiation Oncology/2007   |
|                      |                     | -Cheson BD et al/ClinOncol. 1999   |
|                      |                     | -Bruce D/ RadiolClin N Am 46 (2008)  |

#### REFERENCE

- 1. Lin AY, Tucker MA: *Epidemiology of Hodgkin's disease and non-Hodgkin's lymphoma*. In: Canellos G, Lister TA, Sklar JL, Ed. *The Lymphomas*, London: WB Saunders; 1998:43-61.
- 2. Munazza Annis, Abid Rashid: Imaging of abdominal lymphoma. RadiolClin N Am 2008; 46; 265-85
- 3. Bruce D. Cheson: New staging and response criteria for non Hodgkin's lymphoma.RadiolClin N Am 2008; 46; 213–23
- 4. Howard, Middlemiss: Radiology of the future in developing countries; proceedings of the British institute of radiology. BJR 1984; 682; 851-55
- 5. MesfinTsige, Asfaw Atnafu: Status of radiological service in Addis Ababa public hospital. Ethiop Med J 2011:49 (3)
- 6. Cheson BD, Pfistner B, Juweid ME, et al. Revised response criteria for malignant lymphoma. J ClinOncol 2007; 25; 579–86.
- 7. Expert Panel on Radiation Oncology–Hodgkin's Work Group. Follow-up of Hodgkin's disease [monograph on the Internet]. Philadelphia (PA): American College of Radiology2005 Available at:http://www.acr.org/s\_acr/bin.asp?CID=1229&DID=11888&DOC=FILE.PDF
- 8. Cancer Action Ontario. Recommendation report diagnostic imaging in lymphoma; March 2008
- 9. Milkias Shamebo: Pattern of hospital admission in hematologic malignancies: EMJ 25 (3); 113-18
- 10. Rademaker J. Diagnostic imaging modalities for the assessment of lymphoma with special emphasis on CT, MRI and US. PET Clinics 2006;1(3); 219–30
- 11. Mikhaeel NG, Timothy AR, O'Doherty MJ, Hain S, Maisey MN: 18-FDG-PET as a prognostic indicator in the treatment of aggressive Non-Hodgkin's Lymphoma-comparison with CT. Leuk Lymphoma. Nov 2000; 39(5-6);543-53.
- 12. Zinzani PL, Chierichetti F, Zompatori M, Tani M, Stefoni V, Garraffa G, et al: Advantages of positron emission tomography (PET) with respect to computed tomography in the follow-up of lymphoma patients with abdominal presentation. Leuk Lymphoma. June 2002; 43(6);1239-43.
- 13. Munker R, Stengel A, Stabler A, et al: Diagnostic accuracy of ultrasound and computed tomography in the staging of Hodgkin's disease. Verification by laparotomy in 100 cases. *Cancer* 1995; 76; 1460-1466.
- 14. Esoro-Tess JD, Balzarini L, Ceglia E, Petrillo R, Santoro A, Musumeci R. Magnetic resonance imaging in the initial staging of Hodgkin's disease and non-Hodgkin lymphoma. Eur J Radiol. Mar-Apr 1991; 12(2); 81-90.
- 15. Mattew J Matasar, Andrew D Zelenetz: Overview of lymphoma diagnosis and management. RadiolClin N Am 2008; 46; 175–198.
- 16. Vassallo P, Wernecke K, Roos N, Peters PE: Differentiation of benign from malignant superficial lymphadenopathy: the role of high-resolution US. Radiology 1992; 183; 215-20.
- 17. Carroll BA: Ultrasound of lymphoma. Semin Ultrasound 1982; 3(2); 114-22
- Masahiro Okada, Norihide Sato, Kazunari Ishii, Kaname Matsumura, Makoto Hosono, Takamichi Murakami. FDG PET/CT versus CT, MR imaging and 67 GaScintigraphy in the post theraphy evaluation of malignant lymphoma; RadioGraphics 2010; 30;939–57
- 19. Tschammler A, Hahn D. Multivariate analysis of the adjustment of the colour duplex unit for the differential diagnosis of lymph node alterations. EurRadiol 1999; 9:1445-50.
- 20. Giovagnorio F, Galluzzo M, Andreoli C, De CM, David V. Color Doppler sonography in the evaluation of superficial lymphomatous lymph nodes. J Ultrasound Med 2002; 21; 403-408.
- 21. Schulte-Altedorneburg G, Demharter J, Linne R, Droste DW, Bohndorf K, Bucklein W. Does ultrasound contrast agent improve the diagnostic value of color and power Doppler sonography in superficial lymph node enlargement? Eur J Radiol 2003; 48; 252-57
- 22. Goerg C, Schwerk WB, Goerg K. Sonography of focal lesions of the spleen. AJR 1991; 156; 949-53
- 23. Schoder H, Noy A, Gonen M, et al: Intensity of 18fluorodeoxyglucose uptake in positron emission tomography distinguishes between indolent and aggressive non-Hodgkin's lymphoma. J ClinOncol 2005; 23; 4643-51
- 24. Mikosch P, Gallowitsch HJ, Zinke-Cerwenka W, et al: Accuracy of whole-body 18F-FDP-PET for restaging malignant lymphoma. Acta Med Austriaca 2003; 30; 41-47.
- 25. Rankin SC: Assessment of response to therapy using conventional imaging. Eur J Nucl Med Mol Imaging 2003;30(Suppl 1):S56–64.

- 26. Lister TA, Crowther DM, Sutcliffe SB, et al: Report of a committee convened to discuss the evaluation and staging of patients with Hodgkin's disease: Cotswold's meeting. J Clin Oncol 1989; 7;1630–6.
- 27. Canadian Association of Radiologists. Diagnostic Imaging referral guidelines. 2005. http://www.car.ca/ethics/guidelines/index.html
- 28. Cheson BD, Horning SJ, Coiffer B, Shipp MA, Fisher RI, Conners JM, et al: Report of an international workshop to standardize response criteria for non-Hodgkin's lymphoma. J ClinOncol. 1999; 17(4); 1244-53.
- 29. American college of Radiology, appropriateness criteria: June 2000, volume 215; 1269-279

#### CASE REPORT

# PATENT VITELLINE DUCT WITH GANGRENOUS SMALL BOWEL PROLAPSE: CASE REPORT AND REVIEW OF LITERATURE

Amezene Tadesse, MD<sup>1</sup>, Philipos Kidane, MD<sup>1</sup>

#### **ABSTRACT**

Vitelline duct anomalies (VDA) are rare complications of persistent omphalomesentric duct or vitelline duct connecting the developing embryo with the yolk sac. VDA can be asymptomatic (detected incidentally) or symptomatic, most common of which is Meckel's diverticulum. A patent vitelline duct is the most common symptomatic presentation in African children and we present here a four day old neonate with patent vitelline duct with ileal prolapse. The neonate was operated with the patent vitelline duct and gangrenous ileum resected and end to end ileal anastomosis done.

## **INTRODUCTION**

Vitelline duct or omphalomesenteric duct anomalies are secondary to the persistence of the embryonic vitelline duct, which normally obliterates by weeks 5 -9 of intrauterine life. These anomalies occur in approximately 2% of the population and may remain silent throughout life, or may present incidentally sometimes with an intraabdominal complication.

Although Meckel's diverticulum is the most common vitelline duct anomaly, a patent vitelline duct is the most common symptomatic presentation in developing countries (1).

#### Case presentation:

A four day old female neonate was admitted to our neonatal ward after presenting with protruding mass through the umbilicus of one day duration. Mother noticed the mass protruded after the neonate cried excessively. She was passing meconium from first day onwards. She has no history of vomiting. She was born to 28 years old para II lady. The mother had regular antenatal follow up and the pregnancy was uneventful. Labor lasted 12 hrs and the delivery was spontaneous vaginal delivery.

Abdominal examination revealed fleshy pink mass protruding through the umbilical defect. There was a defect at the umbilical area measuring 3 cm in diameter. There was greenish discharge from the limbs of the protruding mass (**Fig.1**). The anal canal is well -formed and patent.



Fig. 1. Prolapsed ileum (T-shaped)

1 Department of Surgery, School of Medicine, Addis Ababa University, email amezenet@yahoo.com, Addis Ababa Ethiopia

She was admitted with the diagnosis of term neonate + macrosomia + vittelline duct anomaly. She was investigated and Hematocrit was 49% and Random blood sugar 90mg/dl.

With the diagnosis of patent vitteline duct with prolapsed ileum, the neonate was operated through circum-umbilical incision. The prolapsed ileum was ischaemic with bluish discoloration (Fig.2). Majority of the prolapsed segment turned pink after warm pack. The intussuscepted ileum was reduced (Fig.3). and the distal limb was found to be gangrenous (Fig. 4) The patent vitteline duct with the gangrenous ileum around 10 cm long was resected and end to end entero-enterostomy and umbilicoplasty done. She had smooth post-operative course and discharged improved on the 8<sup>th</sup> post-operative day.

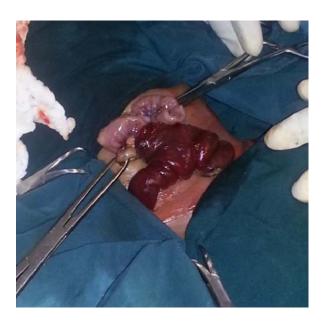


Fig. 2 Ischaemic Ileum just after circumumblical incision

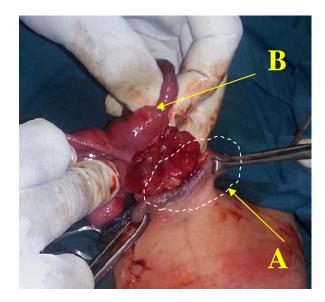


Fig. 3 Intussuscepted ileum being reduced A -The wide patent vitteline duct B - Intussuscepted ileum



Fig. 4. Gangrenous ileal segment after reduction

### **DISCUSSION**

Anomalies of vitelline duct occur as a result of the natural involution of the duct by 9th week of gestation. These anomalies occur in about 2% of the population(1,2). They may be silent throughout life, found incidentally or as a result of complications. The commonest symptomatic presentation is Meckel's diverticulum.

A patent vitelline duct with umbilical faecal drainage is the most symptomatic presentation of vitelline duct anomalies in developing countries(1,2). Other patterns include omphalomesenteric duct (umbilical) sinus, omphalomesenteric duct (umbilical) cyst, umbilical mucosal polyp, or a fibrous cord connecting the ileum to the umbilicus (3,4). Associated congenital anomalies include umbilical hernia, intestinal atresias, cardiac malformation, cleft lip and palate, Exomphalos, trisomy 13 and Down's syndrome(5).

Symptoms include abdominal pain, rectal bleeding, intestinal obstruction, umbilical drainage and umbilical hernia. About 6 % of these anomalies represent a patent duct and 20 % of such ducts being complicated by intussusception of the small intestine. (6) 73 % of such prolapse cases are detected during the neonatal period (6,7). The other more severe complication of such cases would be the progressive prolapse of the duct with a T or Y shaped small bowel protrusion via the umbilicus leading to mucosal ulceration and in severe cases gangrene as is evident in our case where about 10 cm of the distal prolapsed ileum was gangrenous (8, 9).

These anomalies occur in equal frequency in both males and females but the incidence of symptomatic cases is higher in males with a male to female complication ratio of 3:1(2). As has been mentioned above the presence of totally patent duct with prolapsed intestine is exceedingly rare and few cases have been reported so far indicating the rarity of the condition.

Diagnosis is often with history and Physical examination usually done during the initial neonatal evaluation at birth and rarely is further investigations like ultrasound, fistulography and plain abdominal xray needed in complex cases (2). Hence initial thorough evaluation is vital in diagnosing such rare vitellointestinal duct anomalies and further prevents late presentation of such complicated cases of intestinal gangrene and obstruction as is seen with our neonate who presented late with ileal gangrene. Management of such anomalies need to be individualized as to the various patterns of presentation and anomalies and in emergency cases such as our neonate involves initial resuscitation followed by laparotomy often using infra- or circum- umbilical incision, duct resection and end-to-end ileloileal anastomosis(10).

Conclusion: Although rare Vitelline duct anomalies do occur and when symptomatic usually involves Meckel's diverticulum but the other less frequent variants such as the one reported here, patent duct with intestinal prolapse, could have lethal outcomes with complications like intestinal obstruction and gangrene if not detected during the initial neonatal evaluation. Management should include immediate laparotomy and resection of patent ducts after resuscitation.

#### **ACKNOWLEDGEMENT**

We would like to acknowledge Dr Abeje Chane for his role in the management and retrieval of patient information.

#### REFERENCES

- 1. Ameh EA, Mshelbwala PM, Dauda MM, Sabiu L, Nmadu PT. Symptomatic vitelline duct anomalies in children. South Afr J Surg2005; 43:84–85.
- 2. Kurt P, Schropp, MD. Meckel'sdiverticumum. In: Ashcraft K, Holcomb GW III, Murphy JP, eds. Pediatric Surgery. Elsevier Saunders, 2005, Pp 553–557.
- 3. Kuremu R, Jumbi G. Adhesive intestinal obstruction. East Afr Med J 2006;83:333-336
- 4. Moore TC. Omphalomesenteric duct malformations. SeminPediatrSurg 1996;5:116-123.
- 5. Blair S P, Beasley S W. Intussusception vitello-intestinal tract through and exomphalos in Trisomy 13. PediatrSurgInt 4: 422-423, 1997.
- 6. Elebute E A, Ransome-Kuti O. Patent, vitello-intestinal duct with ileal prolapse. Arch Surg 91:456-60, 1965

- 7. Soutar SF, Douglas DM, Dennison WM. Patent vitello–intestinal duct: the risk of obstruction due to prolapse. Br J Surg 45: 617-20, 1958.
- 8. Yamada T, Seiki Y, Ueda M, et al. Patent omphalomesentericduct : a case report and review of Japanese literature. Asia Oceania J ObstetGynaecol 15: 229-36, 1989.
- 9. Prashant N Mohite, Ashok M Bhatnagar, Virsing P Hathila1 and Jitendra H Mistry. Patent vitellointestinal duct with prolapse of inverted loop of small intestine: a case report Journal of Medical Case Reports 2007, 1:49 doi: 10.1186/1752-1947-1-49
- 10. Vane D, West K, Grosfeld J. Vitelline duct anomalies. Experience with 217 childhood cases. Arch Surg 1987;122:542-7

.

#### INSTRUCTIONS TO AUTHORS

The Ethiopian Medical Journal (EMJ) publishes papers containing original observations or research of relevance to clinical medicine and public health. It is the official Journal of the Ethiopian Medical Association (EMA). Prospective contributors to the Journal should take note of the instructions of Manuscript preparation for Articles submitted to EMJ, for publication.

# Article Types accepted by EMJ:-

- 1. Original Articles as reports of current clinical study, retrospective analysis of Hospital records or laboratory research with clinical relevance, not previously published or submitted elsewhere in print or electronic format.
- 2. Case series, Brief communications.
- 3. Review or Teaching Articles; literature review; review of a Medical Book, Pertinent to Africa: by invitation of Editorial Board.
- 4. Editorials.: by invitation of Editorial Board
- 5. Correspondence: regarding Articles appearing in the Journal;
- 6. Monographs/Special issues of the Journal.

## General Instructional information

- All manuscripts must be submitted to the Chairman of the Editorial Board.
- The language of the Journal is **English.**
- Manuscripts must be type-written, on one side of A4 paper; doubt spaced with 2.5cm margin on each side. Submit three copies of the manuscript, with complete References, Tables and Figures.
- 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.
- Abbreviations must be given in full, at first mention in the text and at the foot of Tables, if used in tables.eg. Blood Urea Nitrogen (BUN). Interstitial lung disease ('LD).
- The binomial nomenclature reference to bacteria is used e.g. *HaemophilusInfluenza*
- Accepted papers are subject to Editorial revision as required and become the copyright of the EMA

Preparation of manuscripts and the **format** for each category is as follows:

# **Original Articles:**

About 2500 words, excluding Abstracts, References, Figures and Tables. The manuscript of the Article, should appear under the following headings:

- a) Abstract (see below) b) Introduction and Background: to provide necessary information and background to the Topic. It should not be a review of the subject c) Materials & Methods: should contain details to enable validation of the study by others. Ethical aspect of the study is included in this section. It should be a statement certifying that all applicable institutional and government regulations for Ethical practice were followed in the conduct of the study. Photos of patients should be disguised or have a written consent; d) Results: This section should present the experimental or clinical data in text, tables or figures. The data in Tables and Fig54 ures should not be described extensively in the text. e) 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.
- **Abstracts** of the Article is prepared on a separate paper; about 250 words; it should be structured under the titles: a) **Aims/Purpose**; 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.
- **The Title page** of the Article should be on a separate page of no more than 50 characters. It should be descriptive. Include the name(s), qualification of the author(s); the department or Institution to which the study/research is attributed; address of the main author to whom correspondence should be addressed
- **Tables and Figures** should not be more than six. Three dimensional histograms are discouraged. Tables should be typed in triplicate on separate sheets and given serial Arabic numbers. They should be titled and labeled clearly. Unnecessary and lengthy tables and figures are discouraged. 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.
- **Acknowledgements:** Appropriate recognition of contributors to the research, not included under Authors; also add a note about financial or research funding.
- References:-
- 1. The accuracy of the References is the authors' responsibility.
- 2. References should be listed in order of appearance in the text of the manuscript, as per Vancouver style. Type the References on a separate sheet, double spaced and keyed to the text Abbreviation of Journal titles should conform to that in *Index Medicus*. Provide the first and last pages of each reference.
- 3. While personal comments or unpolished observation are cited in the text in paren thesis, published abstracts can be referenced.
- 4. References with six or less authors should all be listed. If more than six names, list the first three, followed by: *et* al

*The* following examples demonstrate the various Reference styles.

#### A) Articles

- 1. Bill A; Aqueous humor dynamics in monkeys (Macacairis and Cercopithecusethiops) Exp Eye Res 1971; 11:195-206
- 2. Gilbert C, Foster A. Childhood blindness in the context of Vision 2020: the right to sight. Bull World Health Org 2001; 79:227-32
- 3. Bayu Teklu. 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
- 4. Edemariam Tsega; Biru Mengesha; Eric Nordenfelt; Bengt-Goran Hansen; Johan lindberg. Serological survey of Human Immunodeficiency virus infection in Ethiopia. Ethiop Med J 1988; 26(4): 179-84
- 5. Laird M; Deen M; Brooks S et al Telemedicine diagnosis of Diabetic Retinopathy and Glaucoma by direct ophthalmoscopy (Abstract). Invest Ophthalmol Vis Sci1996; 37:104

# B. Books and chapters from books

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

# c) Website

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

## 2. Case Series/Brief Communication:

Minimum of three and maximum of 20 case reports;

- 750 words; excluding: Abstract, Title, Tables and References;
- Abstract of 200 words; structured; (vide supra)
- Statistical statements here are expressed as 5/8 (62.5%)
- References: maximum of 12
- Tables and Figures: no more than three.

# 3. Review Articles:

- By invitation of the Editorial Board; but an outline of proposal can be submitted.
- The chosen topic must be a comprehensive analysis of a specific subject, considered as relevant to clinical medicine and Public Health;
- Word limit of 8000; excluding abstract, references, tables and Figures.
- Unstructured Abstract of 25Owords;
- Reference: maximum of 100.
- **4. Editorial:** by invitation, but an outlined editorial topic can be proposed and submitted. Word limit of 1000 words: excluding references and title; no Abstract; references: maximum of 25.

#### Manuscript Review/action Procedure

- The Editorial Board reserves the right of the final acceptance, rejection or editorial correction of papers submitted.
- Twenty-five reprints are supplied free to the first/corresponding author.
- Authors can submit the peer-reviewed, accepted manuscript to their institution the research funding body or on their web-site, only after publication of the article in the EMJ.

#### **ACKNOWLEDGEMENTS**

We gratefully acknowledge the financial support from US Centers For Disease Control and Prevention (CDC), in accordance to the EMA-CDC Cooperative Agreement No. 5U2GPS000834.

Opinions expressed in any part of the contents of the Ethiopian Medical Journal are not necessarily the opinion of the Board of Editors nor of the Ethiopian Medical Association.

#### THE ETHIOPIAN MEDICAL JOURNAL

The *Ethiopian Medical Journal*, founded in 1962, appears four times a year and is available from the Secretary, EMA House, Addis Ababa, or by mail P. O. Box 3472, Addis Ababa, Ethiopia. Request for previous issues is welcome. For any other information please contact us through:

e-mail: emj@ethionet.et

Tel. 251--1-5533742 or 5521776 Fax: 251-1-5533742

The Journal contains original articles and research of special relevance to health and medicine in Ethiopia and in other developing countries. It is listed in the *Index Medicus* and *Current Contents*. Its ISSN number is ISSN 0014–1755

If you wish to subscribe to the Journal, please complete the section below, and return it to the Secretary. The Subscription rates are:

| Ethiopia: Eth. Birr 372 birr annually, postage included; World-wide: US\$ 120, airmail postage included  |
|--|
| To: The Secretary, <i>Ethiopian Medical Journal</i> , P. O. Box 3472, Addis Ababa, Ethiopia. I wish to subscribe to the <i>Ethiopian Medical Journal</i> for the Year (s) to .  Name |
| Address  |
| I enclose my subscription fee of   |
| Cheques should be made payable to the <i>Ethiopian Medical Journal</i> . If payment is made by Bank Transfer (A/C No. 0172018004100,   |
| Commercial Bank of Ethiopia, Addis Ababa Branch), please ensure that the Secretary of the Ethiopian Medical Journal is notified of the transfer.                                     |
|  |
| . NOTICE TO MEMBERS OF THE ETHIOPIAN MEDICAL ASSOCIATION   |
| If you are a paid—up member of EMA, and have not received your copy of EMJ, please notify the secretary, with the support of your  |
| ID card or letter from your hospital. Also, if you are transferred to a different hospital or institution, please return the   |
| following change of address form <b>PROMPT-LY</b> .  |
| NAME (in block)  |
| P. O. BOX CITY/TOWN  |
| NEW ADDRESS  |
| INSTITUTION  |

P. O. BOX ...... CITY/TOWN .....