



Chief Editor:
Ahmad Husari

Ethics Editor and Publisher:
Ms Lesley Pocock
medi+WORLD International
11 Colston Avenue
Sherbrooke, Vic Australia 3789
Phone: +61 (3) 9005 9847
Fax: +61 (3) 9012 5857
Email:
lesleypocock@mediworld.com.au

Editorial enquiries:
editor@me-jim.com

Advertising enquiries:
lesleypocock@mediworld.com.au

While all efforts have been made to ensure the accuracy of the information in this journal, opinions expressed are those of the authors and do not necessarily reflect the views of The Publishers, Editor or the Editorial Board. The publishers, Editor and Editorial Board cannot be held responsible for errors or any consequences arising from the use of information contained in this journal; or the views and opinions expressed. Publication of any advertisements does not constitute any endorsement by the Publishers and Editors of the product advertised.

The contents of this journal are copyright. Apart from any fair dealing for purposes of private study, research, criticism or review, as permitted under the Australian Copyright Act, no part of this program may be reproduced without the permission of the publisher.

2 Editorial
Ahmad Husari

Original Contribution / Clinical Investigation

- 3 Urinary Tract Infection in Febrile Children below Two Years**
Hussein H Dmour, Hussein M Al-Sa'eed, Mohammad Rwalah, Adnan R Zayadeen
- 7 Effect of Long Term Prophylaxis of Antimalarial Drug (Doxycycline) on Liver Span by Ultrasound**
Adnan R. Zayadeen, Jameel S. Shawagfeh, Hussein H Dmour, Maysoon A. Bani Hani
- 12 Citrullus colocynthis as a bioavailable source of β -sitosterol, antihyperlipidemic effect of oil in rabbits**
Namama S. Talabani, Diary I. Toftiq
- 17 Presentation and Outcome of Strabismus in Adults**
Ismat Ereifej

Community Care

- 20 Screening for chromosomal abnormalities by maternal age and fetal nuchal translucency thickness: The Jordanian experience**
Vera N. Amarin, Hussein M. Alsaied, Hussein h. Dmour, Fatmeh Al Quran
- 25 The Evaluation of the Patients Admitted With Hypoglycemia in an Emergency Department: From the Perspective of an Emergency Specialist**
Huseyin Cebicci, Ali Karakus, Cumali Gokce, Sedat Motor, Cem Zeren Murat Yucel, Nurullah Gunay, Rami Helvaci

Office Based Medicine

- 28 Primary Lymphoma of the Uterine Cervix: A Case Report**
Mohammad Al Quddah

From the Editor



Ahmad Husari (*Chief Editor*)
Email: editor@me-jim.com

This is the first issue of the journal this year. The Middle East journal of internal medicine has achieved major milestones during previous year with the help of the readers, editorial board, authors and publishing company.

In this issue a number of papers from the region dealt with important topics in the field. A paper from Turkey evaluated hypoglycemia in the emergency department. This study was carried out at the Department of Emergency Medicine (EM) in a Training and Research Hospital, and 5,000 consecutive patients admitted to EM were enrolled. They were evaluated in aspects of hypoglycemia by clinical and biochemical investigation. Of these patients, 35 of them (females 16, males 19) were diagnosed as having hypoglycemia. The most common cause of hypoglycemia is due to inappropriate diabetic drug usage in 32 (91%) cases with diabetes mellitus (DM), and most of them 24 (68%) were insulin using diabetic patients. The authors concluded that the prevalence of hypoglycemia was approximately 0.7% in patients with DM admitted to EM. The diminished prevalence of hypoglycemia in comparison to the previous reports may be due to qualified patient education and management such as glucometers and insulin pumps.

A paper from Kurdistan Iraq did a phytochemical study on the seed and kernel of *Citrullus colocynthis*. The results revealed the presence of the β -sitosterol in the kernel and seed in different percentages (seed contained 16.92%, and the kernel contained 6.62%). The lipid lowering active compound (β -sitosterol) has been detected by using TLC, IR, UV and H1-NMR. The present study was designed to reveal the hypocholesterolemic effect of β -sitosterol on serum total cholesterol and triglyceride in rabbits. A significant drop in serum total cholesterol and triglyceride was observed at 120 hours, after first administration. These results support the suggestion of *Citrullus colocynthis* oil as a treatment for hyperlipidemia.

A prospective study paper from Jordan attempted to determine the prevalence of urinary tract infection in febrile children less than two years. Children younger than 2 years attending the pediatric emergency department between January 2009 and December 2009 and who had a rectal temperature $\geq 38.5^{\circ}\text{C}$ were included in the

study. A total of 760 patients met the inclusion criteria of the study. Twenty six patients (3.42%) had positive urine cultures. All patients had growth of $\geq 100\,000$ CFU/ml. The authors concluded that prevalence rates increase if there is no definite source of fever, high fever and ill appearance of the child on examination, and the presence of urinary symptoms.

A paper from Jordan attempted to find if there is a significant increase in liver span by ultrasound after 2 and 5 months of using doxycycline 100 mg daily as malaria prophylaxis among the Jordanian contingent working with the United Nations in Liberia. Ultrasound was done to the 115 people in the contingent before starting doxycycline, and repeated after 2 and 5 months. Liver span ranges from 13.6 to 16.8 cm at the beginning. The authors concluded that the increase in liver span after the long term use of doxycycline 100 mg as antimalaria prophylaxis, was statistically not significant (P value 0.00), and it happened mainly in the first two months of using it.

A Case Report from Jordan looked at primary non-Hodgkin's lymphoma (NHL) of the uterine cervix which is an exceedingly rare entity and often poses a diagnostic challenge if its existence is not suspected. Despite typical local manifestation of the genital tract primary NHLs, the uncommon site of this entity may lead to misdiagnosis by pathologists and clinicians who are unfamiliar with the clinical and pathologic features. Because of the low incidence of primary genital tract lymphomas there are no universal protocols regarding treatment. Our patient received multiple courses of chemotherapy and has remained disease free more than a year from the time of diagnosis. The authors concluded that chemotherapy with Cytoxan, Adriamycin, oncovin, mabthera and prednisolone protocol is an effective and tolerable treatment option.

The objectives of a paper on Presentation and Outcome of Strabismus in Adults were to investigate presentation, causes and outcome of strabismus cases in adulthood. A prospective study was conducted at Queen Alia Hospital of the Royal Medical Services looking at presentation and outcome. One hundred and twenty strabismus patients attending the ophthalmology clinic aged over 14 years, were enrolled in the study. A total number of 120 patients were enrolled in the study with age range of 14 years to 78.5 years (mean 34.2 years). Most common cause of presentation was cosmetic concern followed by diplopia. The majority of strabismus surgery in adults are neglected cases from childhood. The main indication for surgery was cosmetic. The outcome of surgery is excellent with rare occurrence of postoperative diplopia.

A paper from Aman looked at the screening for chromosomal abnormalities by maternal age and fetal nuchal translucency thickness.

The risks for trisomy 21 and other chromosomal defects by ultrasound measurement of fetal nuchal translucency thickness and maternal age were calculated, using the software provided by The Fetal Medicine Foundation. Chromosomal defects were diagnosed in 10 cases, including 4 cases of trisomy 21 and 6 cases with other chromosomal abnormalities (trisomy 18, 13, triploidy, Turner). The authors concluded that the combination of maternal age and fetal nuchal translucency thickness was an effective method of screening for chromosomal defects.

Urinary Tract Infection in Febrile Children below Two Years

ABSTRACT

Objectives: to determine the prevalence of urinary tract infection in febrile children less than two years.

Methods: This prospective study was conducted in the Pediatric Emergency Department of Prince Ali Hospital, Jordan. Children younger than 2 years who attended the pediatric emergency department between January 2009 and December 2009 and had a rectal temperature $\geq 38.5^{\circ}\text{C}$, were included in the study. Children with a definite source for fever, immunosuppressed, or on antimicrobial treatment were excluded from the study. Fever was considered a potential cause for urinary tract infection if the child had no evidence of upper respiratory infection, otitis media, gastroenteritis and, non specific skin rash. Urine specimens were obtained for all children included in the study either by transurethral catheterization or suprapubic aspiration by a well qualified pediatric resident using standard sterile technique. Renal ultrasound was also performed for all children included. Prevalence rates with 95% confidence intervals (CIs) were calculated for the study sample and comparison subgroups.

Results: A total of 760 patients met the inclusion criteria of the study. Three hundred and thirty were males and four hundred and thirty were females. The mean age was 11 months. Twenty six patients (3.42%) had positive urine cultures, 21 (80.76%) of these were females and five (19.24%) males. *Escherichia coli* were positive in twenty three (88.5%) patients, two patients had *Enterobacter* and one had *Proteus*. All patients had growth of $\geq 100\ 000$ CFU/ml. Twenty patients (76.9%) had evidence of pyuria (≥ 5 white blood cells per high powered field in spun urine by microscopy). Twenty three (84.6%) were admitted to the hospital and were treated with intravenous antibiotics either before or after culture results. Children who did not have a potential source of fever had higher prevalence (5.74%) than those who had a potential source of fever. Also children who appeared ill on initial examination had higher prevalence (5.73%) than children who appeared well.

Conclusion: Prevalence rates increase if there is no definite source of fever, high fever and ill appearance on examination, and presence of urinary symptoms.

Key words: fever, urinary tract infections, prevalence

Hussein H Dmour
Hussein M Al-Sa'eed
Mohammad Rwalah
Adnan R Zayadeen

Emergency, Pediatric and Radiology Departments,
Prince Ali Ben Al-Hussein hospital, Royal Medical Services,
Jordan

Correspondence:

Adnan Zayadeen MD
Royal Medical Services, Jordan
Email: Dr_adnan1978@yahoo.com

Introduction

The prevalence of urinary tract infection in febrile infants is greater with younger age, with a rate of nearly 7 percent among febrile newborns [1]. Prophylactic antibiotics are usually given to children with febrile urinary tract infections despite there being no evidence that prophylactic antibiotics are protective against development of renal scarring or subsequent long-term medical complications [2, 3].

The classic signs of urinary tract infection and pyelonephritis are not present or easily discerned in the toddler or young child. Fever is the most common symptom of urinary tract infection in the infant [4, 5]. Ascending infections are the most common cause of urinary tract infections in children, although hematogenous spread may be more common in the first 12 weeks of life. Most urinary tract infections in children are monomicrobial, and *Escherichia coli* is the most common pathogen and accounts for about 60 to 80 percent of cases. *Proteus* is more common in boys and in children with renal stones. Other microorganisms that may cause urinary tract infections include *Klebsiella*, *Enterococcus*, and coagulase-negative staphylococci [6].

The aims of this study were to determine prevalence rates of urinary tract infection among young febrile children and to evaluate the effect of age, sex, and clinical symptoms and signs on the prevalence rates of urinary tract infection.

Methods

This prospective study was conducted in the Pediatric Emergency Department of Prince Ali Hospital which is a medium sized regional Hospital in the Southern area of Jordan. Children younger than 2 years who attended the pediatric emergency department between January 2009 and December 2009 and had a rectal temperature $\geq 38.5^{\circ}\text{C}$ were included in the study. Children with a definite source for fever (for example: meningitis, chest infection, septic arthritis, cellulites, and adenitis), who were immunosuppressed, or on antimicrobial treatment, were excluded from the study. Urinary tract infection was considered a potential cause of

fever if the child didn't have upper respiratory tract infection, otitis media, gastroenteritis nor non specific skin rash. Blood culture and malaria tests were done when necessary.

Urine specimens were obtained for all children included in the study either by transurethral catheterization or suprapubic aspiration by a well qualified pediatric resident using standard sterile technique. All specimens were immediately taken to the microbiology laboratory in sterile containers and plated by well qualified laboratory technologists within 10 minutes of receipt using a loop calibrated to deliver approximately 0.001 mL. All plates were incubated at 35°C and examined daily for growth for 2 days. A positive result was defined as growth of a single urinary tract pathogen at $\geq 10^4$ CFU/mL in catheter samples and any number of colonies in suprapubic samples [7]. Renal ultrasound was performed for all children included in the study.

Prevalence rates with 95% confidence intervals (CIs) were calculated for the study sample and comparison subgroups. Comparisons were made between categorical variables using χ^2 test of proportions or, in the case of small samples, Fisher's exact test, with $P \leq .05$ being the a priori significance level.

Results

A total of 760 patients met the inclusion criteria of the study. Three hundred thirty were males and four hundred and thirty were females. The mean age was 11 months. On initial examination, 227 (29.9%) patients appeared ill and, 533 (70.1%) patients were described as well. Urinary tract symptoms included; a history of malodorous urine (2 patients) or hematuria (3 patients); medical history of urinary tract infection or renal anomalies (3 patients); and suprapubic (2 patients), abdominal (15 patients), or flank pain (3 patients) on examination. Potential source for fever was found in 585 (77%) patients. Upper respiratory tract infection and otitis media was seen in 392 (67%), gastroenteritis in 152 (26%), and viral xanthem in 41 (7%).

Twenty six patients (3.42%) had positive urine cultures, 21 (80.76%) were females and five (19.24%) males. *Escherichia coli* were positive in twenty three (88.5%) patients, two patients had *Enterobacter* and one had *Proteus*. All patients had growth of $\geq 100,000$ CFU/ml. Twenty patients (76.9%) had evidence of pyuria (≥ 5 white blood cells per high powered field in spun urine by microscopy). We found that the sensitivity, specificity, positive predictive value, and negative predictive value for standard urine analysis were 77%, 54%, 47%, 53% respectively. Twenty three (84.6%) were admitted to the hospital and were treated with intravenous antibiotics either before or after culture results because thirteen patients appeared ill on initial examination and ten patients had fever $\geq 39.5^\circ\text{C}$ without potential source of fever [Table 1].

Children who did not have a potential source of fever had higher prevalence (5.74%) than those who had a potential source of fever. Also ill appearing children on initial examination had higher prevalence (5.73%) than children who appeared well. A total of 198 males were circumcised because circumcision just for males, during the first month of life is

a habit in our society unless there is a medical indication to prevent or delay circumcision.

Renal ultrasound finding was dilatation of pelvi-calycial system in thirty two patients and, horse shoe kidneys in two patients [Table 2].

Discussion

Urinary tract infection is considered the most commonly diagnosed serious bacterial infection, with prevalence varying from 1.8% to 7.5% [8-10]. Urinary tract infection is often associated with vesicoureteral reflux or urinary tract obstruction [4]. These conditions are associated with a higher risk of recurrent urinary tract infection [11]. Children with urinary tract infection are at risk for renal scarring [12-13], which is one of the most common causes of end-stage renal disease in children [14-15].

In this study, the overall prevalence of urinary tract infection in febrile children less than two years was 3.4%. Although the prevalence of urinary tract infection is higher in children without any other potential source of fever, we found a 2.74% (95% CI: 1.42, 4.06) prevalence in febrile infants with a possible source of fever compared with 3.5% (95% CI: 1.8, 5.2) prevalence rate in another study [16]. Roberts et al. studied children younger than 2 years of age who presented with upper respiratory tract infection or gastrointestinal symptoms felt by the attending physician to be insufficient to explain fever, or without any source of fever on examination; they found that 4.1% had urinary tract infections [17].

During the initial evaluation, higher fever and ill general appearance were strongly associated with urinary tract infection. Although urinary symptoms were uncommonly elicited, such as changes in the urine odor or hematuria; tenderness of the abdominal, flank, or suprapubic areas on examination; or medical history of urinary tract infection, this group had a higher prevalence rate. Vomiting, diarrhea, and poor feeding are reported in many infants admitted for urinary tract infection [18-19], but the prevalence rate of urinary tract infection is not high in this group. A total of 198 males were circumcised because circumcision just for males during the first month of life is a habit in our society, unless there is a medical indication prevent or delay circumcision.

The definition of urinary tract infection used in the current study was based on urine culture results. We did not use urinalysis or dipstick results as criteria for obtaining or interpreting urine cultures. We used growth of 10000 CFU/mL from a catheterized specimen or any growth in suprapubic specimens as a threshold. Standard urinalysis and urine dipstick techniques have relatively low sensitivity (65%-88%) [20, 21]. The presence of pyuria 5 WBC/HPF has been found to be a poor predictor of a positive urine culture [22-24]. The sensitivity, specificity, and positive predictive value of the standard urine analysis are so low that only a third to half of patients with positive urine culture results can be identified correctly [22-24]. In our study, we find that the sensitivity, specificity, positive predictive value, and negative predictive value were 77%, 54%, 47%, 53% respectively. Dukes [25-26]

			N	Percent Prevalence (95% CI)
Overall			760	3.42 [2.1, 4.7]
Sex	Girls		430	4.88 [2.8, 6.9]
	Boys		330	1.52 [0.2, 2.8]
Age/sex	Boys	<12 Mo	251	1.59 [0.04, 3.1]
		≥12 Mo	79	1.27 [-1.2, 3.7]
	Girls	<12 Mo	327	5.5 [3.0, 7.8]
		≥12 Mo	103	2.91[-0.34, 6.2]
Potential source of fever	Yes		585	2.74 [1.4, 4.1]
	No		175	5.71[2.3, 9.2]
General appearance	Well		533	2.44[1.13, 3.75]
	Ill		227	5.73 [2.71, 8.75]
Fever	≥ 39°C		517	3.87 [2.2, 5.5]
	< 39°C		243	2.47 [0.52, 4.4]
Any tenderness on examination	Yes		55	14.55 [5.2, 23.9]
	No		705	2.55 [1.4, 3.7]
Medical history of UTI*	Yes		21	12.55[-3.03, 22.1]
	No		739	3.25 [1.97, 4.53]
urinary symptoms	Yes		60	13.33 [4.7, 21.9]
	No		700	2.57[1.4, 3.74]

*UTI: urinary tract infection

Table 1

	No.	%
Normal U/S	668	87.9
Dilated pelvicalyceal system	32	4.2
Thickening U.B wall	58	7.6
Horseshoe kidney	2	0.3

Table 2: Ultrasound findings

described a more accurate microscopic analysis of un-centrifuged urine performed with a hemocytometer and reporting cells per cubic millimeter, herein referred to as hemocytometer white blood cell (WBC) counts.

Conclusion

As in other studies, urinary tract infection should be considered in febrile infants. Prevalence rates increase if there is no definite source of fever, high fever and ill appearing child on examination, and presence of urinary symptoms.

References

- Bachur R, Harper MB. Reliability of the urinalysis for predicting urinary tract infections in young febrile children. *Arch Pediatr Adolesc Med.* 2001;155:60-65.
- Ghiro L, Cracco AT, Sartor M, et al. Retrospective study of children with acute pyelonephritis. *Nephron.* 2002;90 (1):8-15.
- Smith J, Finn A. Antimicrobial prophylaxis. *Arch Dis Child.* 1999;80 (4):388-392.
- Winberg J, Andersen HJ, Bergstrom T, et al. Epidemiology of symptomatic urinary tract infection in childhood. *Acta Paediatr Scand.* 1974;252:1-20.
- Ginsburg CM, McCracken GH. Urinary tract infections in young infants. *Pediatrics.* 1982; 69:409-412.
- Twaij M. Urinary tract infection in children: a review of its pathogenesis and risk factors. *J R Soc Health.* 2000;120:220-226.
- Hellerstein S. Recurrent urinary tract infections in children. *Pediatr Infect Dis.* 1982; 1:271-281
- Baker MD, Bell LM, Avner JR. Outpatient management without antibiotics of fever in selected infants. *N Engl J Med.* 1993;329 :1437-1441.
- Baskin MN, O'Rourke EJ, Fleisher GR. Outpatient treatment of febrile infants 28 to 89 days of age with intramuscular administration of ceftriaxone. *J Pediatr.* 1992;120 :22-27.
- Jaskiewicz JA, McCarthy CA, Richardson AC, et al. Febrile infants at low risk for serious bacterial infection-an appraisal of the Rochester criteria and implications for management. Febrile Infant Collaborative Study Group.

Pediatrics. 1994;94 :390 -396.

11. Wallace DMA, Rothwell DL, Williams DI The long term follow-up of surgically treated vesicoureteric reflux. *Br J Urol* 1978; 50:479-484.

12. Holland NH, Jackson EC, Kazee M, Conrad GR. Relation of urinary tract infection and vesicoureteral reflux to scars: follow-up of thirty-eight patients. *J Pediatr.* 1990;116:65-71.

13. Rushton HG, Majd M, Jantausch B, Wiedermann BL, Belman AB Renal scarring following reflux and nonreflux pyelonephritis in children: evaluation with 99mtechnetium-dimercaptosuccinic acid scintigraphy. *J Urol* 1992; 147:1327-1332

14. Heale WF. Hypertension and reflux nephropathy. *Aust Pediatr J* 1977; 13:56

15. Jacobson SH, Eklof O, Eriksson CG, et al. Development of hypertension and uremia after pyelonephritis in childhood: 27 year follow up. *Br Med J* 1989; 299:703-706.

16. Hoberman A, Han-Pu C, Keller DM, et al. Prevalence of urinary tract infection in febrile infants. *J Pediatr.* 1993; 123:17-23.

17. Roberts KB, Charney E, Sweren RJ, Urinary tract infection in infants with unexplained fever: a collaborative study. *J Pediatr.* 1983; 103:864-867.

18. Hoberman A, Wald ER, Reynolds EA, et al. Is urine culture necessary to rule out urinary tract infection in young febrile children? *Pediatr Infect Dis J.* 1996; 15:304-309.

19. Slosky DA, Todd JK. Diagnosis of urinary tract infection. *Clin Pediatr.* 1977; 16:698-701.

20. Gorelick MH, Shaw KN. Screening tests for urinary tract infection in children: a meta-analysis. *Pediatrics.* 1999;104(5). Available at: www.pediatrics.org/cgi/content/full/104/5/e54

21. Dayan PS, Bennett J, Best R, et al. Test characteristics of the urine Gram stain in infants 60 days of age with fever. *Pediatr Emerg Care.* 2002;18 :12 -14.

22. Kass EH. Asymptomatic infections of the urinary tract. *Trans Assoc Am Physicians* 1956; 69:56.

23. Pryles CV, Eliot CR Pyuria and bacteriuria in infants and children. *Am J Dis Child* 1965; 110:628-635.

24. Crain EF, Gershel JC. Urinary tract infections in febrile infants younger than 8 weeks of age. *Pediatrics* 1990; 86:363-367.

25. Dukes C. Some observations on pyuria. *Proc R Soc Med* 1928; 21:1179.

26. Dukes C. The examination of urine for pus. *Br Med J* 1928; 1:391.

Effect of Long Term Prophylaxis of Antimalarial Drug (Doxycycline) on Liver Span by Ultrasound

ABSTRACT

Objective: To find if there is a significant increase in liver span by ultrasound after 2 and 5 months of using doxycycline 100 mg daily as malaria prophylaxis among the Jordanian contingent working with the United Nations in Liberia.

Materials and methods: Ultrasound was done to the 115 people in the contingent before starting doxycycline, and repeated after 2 and 5 months. Liver span was recorded. A total of twenty four persons were excluded from this study population.

Results: Liver span ranges from 13.6 to 16.8 cm at the beginning. The change in span ranges from -0.1 to 0.5 cm in the first two months and -0.1 to 0.9 cm after 5 months from the zero readings.

The average liver span at zero time was 14.99 cm, and increased to 15.20 after 2 months and to 15.25 after 5 months.

Conclusion: The increase in liver span after the long term use of doxycycline 100 mg as antimalaria prophylaxis, was statistically not significant (P value 0.00), and it happened mainly in the first two months of using it.

Key words: Doxycycline, prophylactic antimalaria, liver span.

Adnan R. Zayadeen
Jameel S. Shawagfeh
Hussein H Dmour
Maysoun A. Bani Hani

Correspondence:

Dr. Adnan Zayadeen, Radiology Specialist,
Queen Alia Hospital,
Amman, Jordan
Email: dr_adnan1978@yahoo.com

Introduction

Malaria, despite being preventable and curable, is a major health problem in Liberia, where there is a high risk for travelers to be infected. It is always a serious disease and may cause death. The most common species is *P. falciparum* (85%). (1)

Malaria is the leading cause of attendance at out-patient clinics (38%) and is also the number one cause of in-patient mortality in Liberia. Hospital records show that at least 42 % of in-patient deaths are due to malaria (NMCP,2006).(2)

Malaria is transmitted through mosquito bites. The symptoms include; fever, chills, fatigue, headache, nausea and vomiting.

Jordan contributes to the UN mission in Liberia by a level III hospital in the capital Monrovia. Malaria prevention techniques are used (insect repellent; long-sleeved clothing; bed net; and flying insect spray) (3, 4). Commonly used antimalarial prophylactic medications are listed in Table 1.(4) Doxycycline was the chemoprophylaxis used in this study at the period February-July 2012.

Doxycycline is a member of the tetracycline antibiotics group (semi-synthetic). The prophylaxis should begin two days before travel to the endemic areas. It is taken once daily, at the same time each day, during travel in endemic areas and continues for 4 weeks after the traveler leaves such areas. (5, 6)

Doxycycline side effects include: Permanent staining of teeth; rash, nausea, GI upsets, diarrhea; dysphagia; heartburn; photosensitivity. Doses greater than 2 g/day are associated with liver failure; making it imperative to monitor function and avoid other hepatotoxic drugs.(5, 6)

This study was conducted to find if there is a significant increase in liver span by ultrasound after 2 and 5 months of using doxycycline 100 mg daily as malaria prophylaxis among the Jordanian contingent in Liberia.

Material and Methods

This is a prospective study, conducted between February till July 2012 on the personnel of the Jordanian contingent in Liberia. The study started with 115 persons. Twelve persons were excluded because they could not tolerate the GI side effects of doxycycline. Ten got malaria infection. Two were using other medications that could affect the liver. Their age range was from 18 to 51 years with a mean age of about 30 years. All are males. Liver ultrasound was done to all of them at the beginning of the study, and repeated after 2 months and 5 months of using doxycycline 100mg tablets daily. So a total of ninety one persons form the study population.

Ultrasound was done by a radiology specialist on Seimens (Acuson CV70) machine. Liver span was recorded for each person at the beginning of the study and after 2 and 5 months. Liver span measured by midclavicular line longitudinal diameter.

When follow up ultrasound was done, the radiologist didn't know the previous span for the person. Data was collected and analysis calculated.

Results

The liver span at zero time ranges from 13.6-16.8 cm, with an average of 14.99 cm.

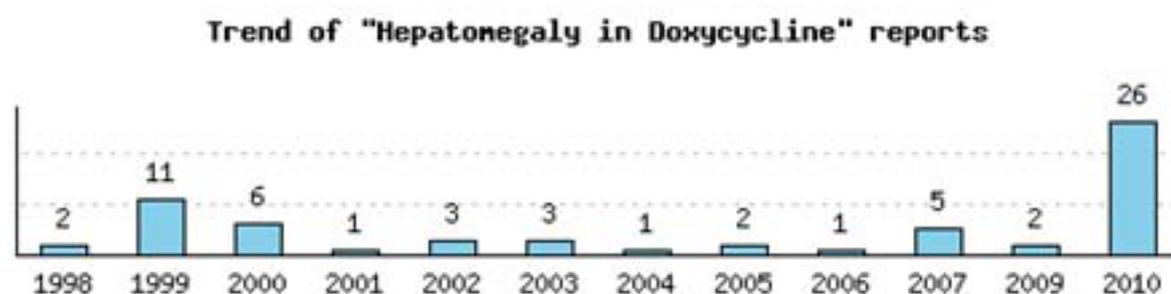


Figure 1

After two months, the average span increased to 15.20 cm. The difference in span ranges from -0.1 cm to 0.5 cm. and after 5 months it became 15.25 cm, and the change ranges from -0.1 to 0.9 cm compared to zero time.

Medication	Dose	Frequency	Resistance for falciparum malaria	Time prior to entering a malarial endemic area	Time after leaving a malarial endemic area
Doxycycline	100mg	daily	No	2 days	4 weeks
Chloroquine	300mg	weekly	Yes	1 week	4 weeks
Mefloquine	250mg	weekly	Yes†	2 weeks	4 weeks

Table 1: Commonly used antimalarial prophylactic medications

According to this we noticed that there was an average increase of 0.21 cm in the first two months and 0.05 cm in the following three months. This increase proved to be statistically insignificant (P value 0.00). (Table 3)

	Zero time	After 2 months	After 6 months				
1	14.2	14.5	14.6	41	14.3	14.5	14.9
2	14.1	14.2	14.3	42	14.3	14.4	14.4
3	14.6	14.6	14.6	43	14.6	14.8	14.9
4	15.1	15.2	15.6	44	15.1	15.4	15.8
5	14.2	14.5	14.4	45	15.5	15.7	15.6
6	14.1	14.4	14.3	46	14.6	14.6	14.5
7	14.2	14.2	14.2	47	15.0	15.0	15.1
8	14.7	14.8	14.7	48	14.2	14.3	14.2
9	14.9	14.9	15.0	49	14.1	14.2	14.4
10	14.5	14.9	14.8	50	14.2	14.3	14.6
11	14.8	14.9	14.8	51	14.6	14.7	14.7
12	14.9	14.9	14.9	52	14.9	15.4	15.3
13	14.2	14.2	14.1	53	14.4	14.6	14.5
14	14.6	14.8	14.7	54	14.7	14.8	14.8
15	15.2	15.4	15.5	55	14.8	14.9	15.0
16	15.0	15.1	15.2	56	14.2	14.5	14.3
17	15.3	15.7	15.4	57	14.6	14.7	14.8
18	15.2	15.5	15.5	58	15.4	15.3	15.5
19	15.1	15.4	15.6	59	15.8	16.0	16.1
20	15.5	15.6	15.7	60	15.9	16.2	16.2
21	15.1	15.2	15.4	61	15.5	15.7	15.8
22	13.9	14.0	14.0	62	15.8	15.9	16.1
23	14.2	14.3	14.4	63	15.6	15.9	15.9
24	15.3	15.5	15.6	64	15.5	15.8	15.8
25	15.2	15.5	15.4	65	16.2	16.7	16.6
26	15.1	15.2	15.1	66	15.4	15.6	15.7
27	16.0	16.3	16.2	67	15.3	15.5	15.8
28	15.7	15.9	15.8	68	16.2	16.4	16.6
29	15.3	15.7	15.6	69	14.9	15.4	15.3
30	15.2	15.4	15.4	70	14.8	15.1	15.2
31	15.3	15.6	15.5	71	14.7	14.9	14.9
32	15.6	15.8	15.7	72	15.0	15.3	15.1
33	15.8	15.8	15.9	73	15.2	15.4	15.7
34	14.2	14.4	14.7	74	16.3	16.5	16.5
35	13.9	14.1	14.4	75	16.3	16.4	16.5
36	14.1	14.4	14.5	76	16.8	17.2	17.3
37	14.4	14.8	14.7	77	14.2	14.5	14.5
38	14.4	14.6	14.5	78	14.8	15.3	15.7
39	14.2	14.6	14.4	79	15.3	15.5	15.4
40	14.3	14.4	14.5	80	15.6	15.7	15.9

(continued next page)

Table 2: Liver span according to time

(continued next column)

(Table 2 continued)

81	15.7	15.9	15.8
82	15.4	15.4	15.5
83	16.4	16.6	16.8
84	16.4	16.6	16.6
85	15.9	16.4	16.3
86	15.7	16.1	16.2
87	15.4	15.5	15.7
88	13.6	14.0	14.2
89	14.7	15.1	15.3
90	14.2	14.5	14.7
91	14.8	15.4	15.3
Average	14.993	15.205	15.252

Discussion

Doxycycline is a member of the tetracycline antibiotics group (semi-synthetic). It works through binding to 30S and 50S ribosomal subunits. It is almost completely absorbed from the GI tract; peak plasma concentrations occur after about 2 hours. Absorption is not significantly affected by food. It is lipid soluble and protein-binding is 80-95 %. It is metabolized in the liver and excreted via urine. Its elimination half-life is 12-24 hours. (5, 6)

Doxycycline is a very effective prophylaxis for chloroquine-resistant *P. falciparum*. It is contraindicated in pregnant or breastfeeding women and children below eight years of age.

There are no known serious adverse events from its long-term use, however daily dosing is a disadvantage and may lead to poor compliance.

Doxycycline is found to have some abnormal effects on liver function tests. Jaundice is found in some cases. Even though it is rare, it is potentially dangerous for those who are affected. Not much is written in the literature about increase of liver span after long term doxycycline prophylactic antimalarial use. Figure 1 shows the trend of hepatomegaly in doxycycline reports over the last twelve years(7). In April 10, 2012: 7,046 people reported to have side effects when taking Doxycycline. Among them, 63 people (0.89%) had Hepatomegaly, and all of these had the hepatomegaly within 1-6 months. No one had hepatomegaly before 1 month or after 6 months.(7)

In this study we concentrate on the liver span changes due to the use of doxycycline antimalarial chemoprophylactics. The study started with 115 young, healthy military persons. All who had factors that may affect liver span were excluded from this study.

Despite that there was mild increase in liver enzymes in some of the study population; the increase in liver span proved to be insignificant.

Conclusion

The increase in liver span after the long term use of doxycycline 100 mg as antimalarial prophylaxis, was statistically not significant (P value 0.00), and it happened mainly in the first two months of using it.

References

- Centers for Disease Control and Prevention, CDC
- Liberia. Malaria indicator survey 2009. http://pdf.usaid.gov/pdf_docs/PNADQ924.pdf
- International Association for Medical Assistance to Travellers. World malaria risk chart. 2008. Available online at: <http://www.iamat.org/pdf/WorldMalariaRisk.pdf>.
- Committee to Advise on Tropical Medicine and Travel. Canadian recommendations for the prevention and treatment of malaria among international travellers. CCDR 2009;35(S1). Available online at: <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/09vol35/35s1/index-eng.php.11>
- Kathrine R. Tan,* Alan J. Magill, Monica E. Parise, and Paul M. Arguin Doxycycline for Malaria Chemoprophylaxis and Treatment: Report from the CDC Expert Meeting on Malaria Chemoprophylaxis Am J Trop Med Hyg. 2011 April 5; 84(4): 517-531.
- 2011 drugsupdate.com
- Could Doxycycline cause Hepatomegaly? - eHealthMe Available online at www.ehealthme.com/ds/doxycycline/hepatomegaly

Notes

21-JUN-2012 08:39:59	Output Created
<none>	Comments
<none>	Filter Input
<none>	Weight
	Split File
93	N of Rows in Working Data File
User defined missing values are treated as missing.	Definition of Missing Missing Value Handling
Statistics for each analysis are based on the cases with no missing or out-of-range data for any variable in the analysis.	Cases Used
T-TEST	Syntax
PAIRS = pre WITH post (PAIRED)	
/CRITERIA = CI(.95)	
/MISSING = ANALYSIS.	
	Elapsed Time Resources
0:00:00.09	

[DataSet0]

Paired Samples Statistics

Std. Error Mean	Std. Deviation	N	Mean	
.07056	.68044	93	14.9934	pre Pair 1
.07325	.70639	93	15.2055	post

Paired Samples Test

Sig.	Correlation	N	
.000	.980	93	pre & post Pair 1

Paired Samples Correlations Paired Samples Test

	Paired Differences				t	df	Sig. (2-tailed)	
	Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
				Lower				Upper
Pair 1 pre - post	-.21209	.14052	.01457	-.24103	-.18315	-14.555	92	.000

Table 3: T-Test

Citrullus colocynthis as a bioavailable source of β -sitosterol, antihyperlipidemic effect of oil in rabbits

ABSTRACT

A phytochemical study on the seed and kernel of *Citrullus colocynthis* has been carried out in the present paper. The results revealed the presence of β -sitosterol in the kernel and seed in different percentages (seed contains 16.92%, and the kernel contains 6.62%). The lipid lowering active compound (β -sitosterol) has been detected by using TLC, IR, UV and ¹H-NMR. The present study was designed to reveal the hypocholesterolemic effect of β -sitosterol on the serum total cholesterol and triglyceride in rabbits. A significant drop in serum total cholesterol and triglyceride was observed at 120 hours after first administration. These results support the suggestion of *Citrullus colocynthis* oil as a treatment for hyperlipidemia.

Key words: *Citrullus Colocynthis*, β -sitosterol, Hyperlipidemia

Namama S.Talabani
Diary I. Tofiq

University of Sulaimani -Faculty of Science and Science
Education Chemistry Dept., Kurdistan, Iraq

Correspondence:

Namama S.Talabani (Msc.Biochemistry)
Email: sareali@hotmail.com
Diary I. Tofiq (Ph.D Bioinorganic Chemistry)
Email: tofiq.diary@gmail.com

Introduction

Citrullus Colocynthis (Cucurbitaceae), commonly known as bitter apple is a tropical plant that grows abundantly in the Arabian countries and in other parts in Asia. In traditional medicine, this plant has been used to treat constipation(1), diabetes(2), antimicrobials (3), oedema, fever, jaundice, leukaemia, bacterial infections, cancer, hair loss treatment (4) and as an abortifacient (5). The root of this plant is given in abdominal enlargements and in coughs and asthmatic attacks in children (6). Oils and fats are substances of vegetable or animal origin. The high world demands for oils and fats to meet the multiplex human consumption and the multitudinous industrial needs are the reasons for the increase in the importance of oil seeds and make them play an important role in the national economy of the producing countries (7).

Sitosterols ($C_{29}H_{50}O$) are widely distributed throughout the plant kingdom, especially of green leaves and they have usual steroid structure sometimes referred to as vegetable cholesterol(8,9).

Preliminary pharmacological investigations prove that β -sitosterol has a moderate anti inflammatory activity (10). On the other hand, β -sitosterol is a hypocholesterolemic agent that acts by decreasing or blocking the absorption of both exogenous and endogenous cholesterol from the gastrointestinal tract and lowering the blood cholesterol level (11,12).

The purpose of our research was the pharmacognostical study of *Citrullus colocynthis* (seed and kernel) cultivated in Iraq, Kurdistan, in order to establish quality criteria of this plant.

Methods

Plant Material:

Citrullus colocynthis fruits were collected from Kurdistan (Northern Iraq), divided in half and the seeds removed by hand from kernel, dried and then powdered mechanically.

The lipid fraction was extracted with petroleum ether (40°-60°) in a soxhlet apparatus. The solvent was evaporated and the lipid fraction was weighed. (Table 1).

Separation of β -sitosterol:

100 ml of alcoholic potassium hydroxide (5% w/v) was added to the oil extract, then refluxed and heated in water bath for 3 hours. The solution was extracted while just warm, three times with ethyl acetate (100 ml), then we poured each ethyl acetate extract into another separator containing (40ml) of distilled water. The acetate extracts were combined, dried Na₂SO₄ poured in to a weighed flask and evaporated; the pale yellow oily materials was weighed (13). (Table 1)

Standard and reagents:

β -Sitosterol (purity 98%) was purchased from Sigma Aldrich chemie GmbH (Aldrich Division, Steinbeim, Germany).

Characterisation of extracts:

Thin layer chromatography was performed on pre coated silica gel-G plates (10×10) (Emerck, Germany) for characterisation of the extract. Cyclohexan-acetone-acetic acid 65:33:2 v/v as mobile phase, gave best resolution for petroleum ether extract. The spots were visualized using 20% H₂SO₄ as derivatising agent. After that we used IR, UV, and H-NMR for identification of β -sitosterol.

Animal:

Male domestic rabbits were used in an experiment in June 2011. The rabbits were adapted for five days before the start

of the experiment. The animals were divided into two groups with approximately the same weight distribution (1.55-1.85Kg) in each group

Group I: control group - 4 rabbits-non treated β -sitosterol

Group 2: tested group - 6 rabbits received 80mg/10ml of β -sitosterol per animal /day

Water suspension of the dried β -sitosterol was given orally using special stomach tube, at 9.00am and 9.00pm every day for a week.

Serum total cholesterol and triglyceride were analyzed by an enzymatic CHOD-POP method using the test kit of bio Me'rieuxsa (69280.Marcy/ France).

Statistical analysis:

All values expressed as mean \pm standard error (SEM). Independent student's test was applied to analyze the significance of differences between mean values and critical p-value were considered to be significant.

Results

The results indicated that citrullus colocynthis seed and kernel contain β -sitosterol (Table 1). To examine the β -sitosterol in oil, a simple TLC has been performed; the solution of standard of β -sitosterol has been used as markers (Table 2). The infrared spectrum of β -sitosterol is shown in Figure 1, while the nuclear magnetic resonance spectrum (H¹-NMR) of β -sitosterol shown in Figure 2. In comparison

Wt of plant	Oil gm	β -sitosterol gm
250 gm Plant kernel	10.49	6.62%
250 gm Plant seed	27.48	16.95%

Table 1: Oil content in the plant

Plant	Solvent	Rf	λ max in CH ₃ OH
Seed	Cyclohexan-aceton-acetic acid (65:33:2)	8.7	278.3
Kernel	Cyclohexan-aceton-acetic acid (65:33:2)	8.7	278.3

Table 2: Property of β -sitosterol TLC

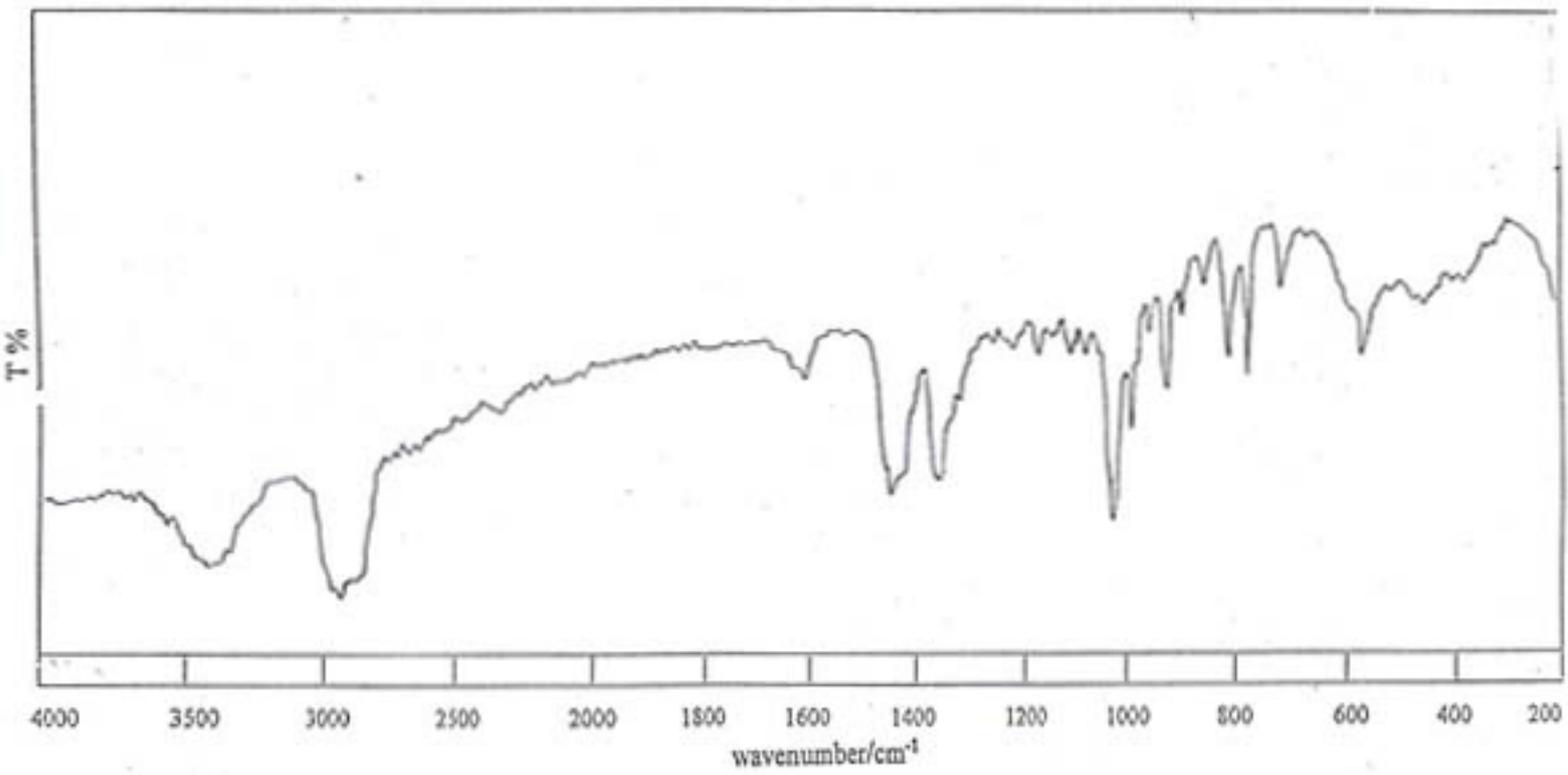


Figure 1: IR spectrum of compound β -sitosterol (B)

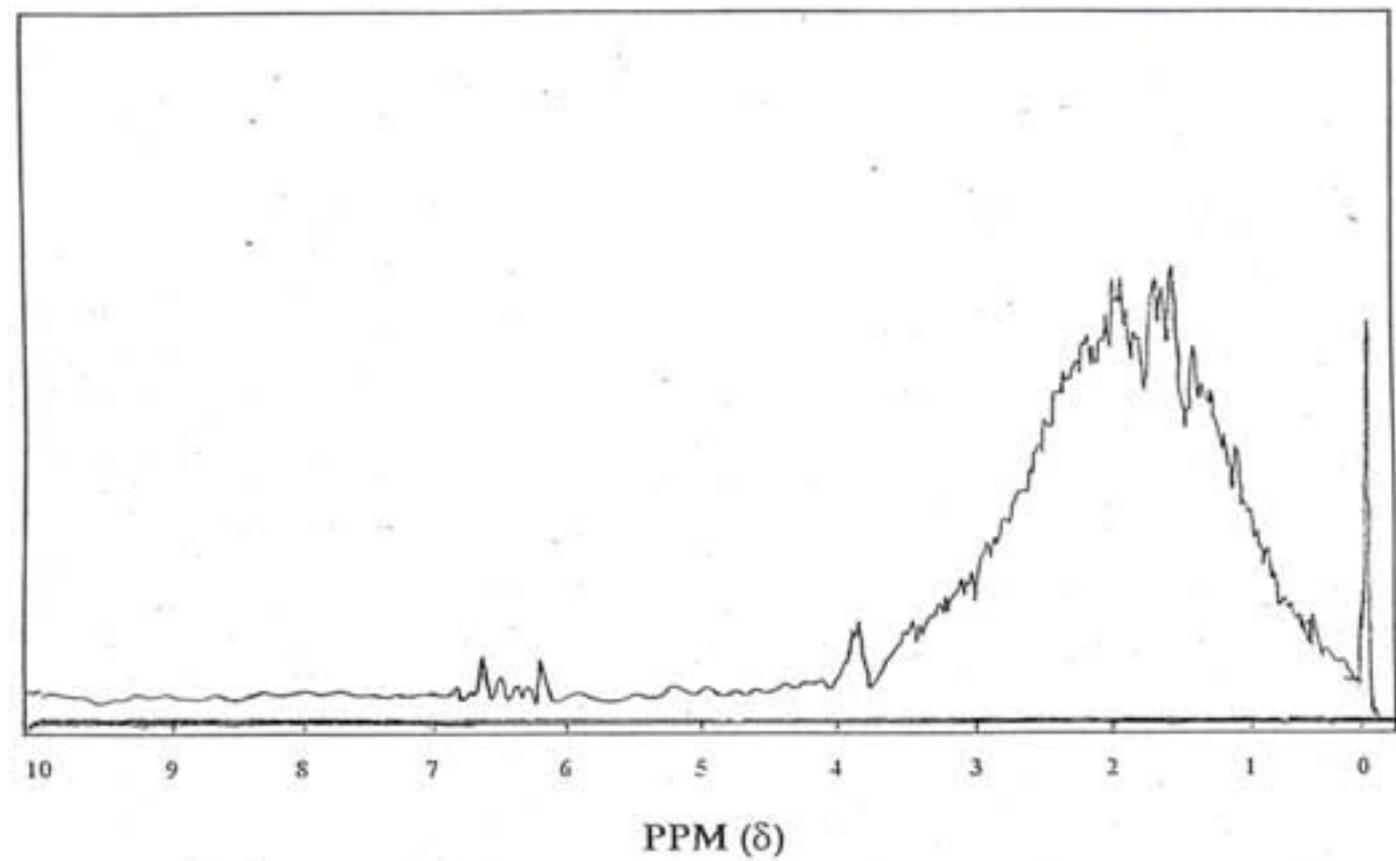


Figure 2: $^1\text{H-N.M.R.}$ spectrum of compound β -sitosterol

Cholesterol	Mean µg/dl	Calculated ±t	Tabulated ±t
Control	89.1	-	
T1	83.4	0.471	3.13
T2	72	2.35	3.13
T3	63	3.12	3.13

Table 3: Statistical analysis of the effect of β -sitosterol on S. total cholesterol

TG	Mean Mg/dl	Calculated ±t	Tabulated ±t
Control	74.35	-	-
T1	68.01	1.07	3.13
T2	44.6	1.81	3.13
T3	37.5	7.25	3.13

T1=48 hrs. after administration (2 days)

T2=96 hrs. after administration (4 days)

T3=120 hrs. after administration (6 days)

Table 4: Statistical analysis of the effect of β -sitosterol on S.triglyceride

between TLC, IR,H-NMR, and UV spectrum , we found that the compound appeared to be β -sitosterol which was isolated from *Citrullus colocynthis*.

After that, the present study was designed to reveal the hypercholesterolemic effect of β -sitosterol of *Citrullus colocynthis* on the serum total cholesterol and triglycerides in rabbits.

A significant drop ($P < 0.01$) in serum total cholesterol and triglyceride was observed, at 120 hours after first administration.(Table 3, Table 4 - page 15).

Quantification of β -sitosterol in petroleum ether extract, shows that the sample of *Citrullus colocynthis* seed (16.95%), contains more β -sitosterol than the kernel of *Citrullus colocynthis* (6.62%).

The results of this study are generally in agreement with those of Bhadra et al(14) and Sato et al (15) in that the β -sitosterol accumulation caused a significant reduction in the cholesterol content of the cell.

The present experiments lead us to the conclusion *Citrullus colocynthis* has an antihyperlipidemic effect and this property is due to the presence of β -sitosterol.

Further studies are in progress in our laboratory to isolate the active compounds in this plant which is found in North of Iraq (Kurdistan region).

References

- 1- Alkofahi A, Batshoun R, et al. Biological activity of some Jordanian plants extracts. *fitoterapia* 1996;5:435-42
- 2- Gurudeeban S, Ramanathan T, Antidiabetic effect of *Citrullus colocynthis* in alloxan-induced diabetic rats. *Inveuti rapid: Ethno pharmacology* 2010,1:112
- 3- Gurudeeban S, Ramanathan T, Satyavani K and Dhinesh T. *African journal of pure and applied chemistry* 2011,vol 5(5):119-122
- 4- Roy RK; Thakur, Mayank Dixit, V.K. Effect of *Citrullus colocynthis* schrad. On hair growth activity of albino rats. *Australian J. of medical herbalism.* 2007;18:980-987
- 5- Madari H, Jacobs R. An analysis of cytotoxic botanical formulation used in the traditional medicine of ancient Persia as abortifacient. *J. Nat prods* 2004;67:1204-10
- 6- Hakeem Brohi U.M, Syed Waseemuddin. *Pak J of pharm sci.* 2003; 16(1):1-6
- 7- Charly H,1982. *Food science*,2nd ed New York; John Wiley and Sons publishers,91-95.
- 8- Fruton Simmonds, *General Biochemistry* 2nd ed 1963
- 9- Eduard P. Glous and Varro E. Tylor, *J pharmacognosy* 5th ed. Philadelphia,1968.
- 10- Senatore AT, Watkins -WD; Nguyen TD. *Toxicol appl. Pharmacol.* 1989(15);99 (2): 357-361.
- 11- Murrar, Ganner, Mayes, Rodwell. *Harper's Biochemistry* 24th ed 1996.
- 12- James M. Ortenlottow. *Neuhaus. Human Biochemistry* 9th ed . Saint louis 1975.
- 13- Butterworth and Copublisher, Pearson, *Laboratory Techniques in food analysis* ,London 1973.
- 14- Bhadra S: Subbiah MT,*Biochem-Med-Meta-Biol.* 1991;46(1):119-124.
- 15- Sato Y; Nishikawa K; Aikawa K; Arai H; *Biochem biophys Acta* 1995;27;1257(1):38-46.

Presentation and Outcome of Strabismus in Adults

ABSTRACT

Objectives: To investigate presentation, causes and outcome of strabismus cases in adulthood.

Patient and methods: A prospective study that was conducted at Queen Alia Hospital of the Royal Medical Services during the period between August 2010 and August 2012. One hundred and twenty strabismus patients attending the ophthalmology clinic aged over 14 years, were enrolled in the study. Patients were asked about onset of strabismus and symptoms complained of. Ophthalmologic examination included best corrected visual acuity, orthoptic assessment, anterior and posterior segment examination. The type of treatment, whether medical or surgical, was recorded. Complications of surgery were also recorded.

Results: A total number of 120 patients were enrolled in the study with age range of 14 years to 78.5 years (mean 34.2 years). Male to female ratio was 1.1 to 1. Sixty six patients (55%) had exotropia, 36.7% had esotropia and 8.3% had hypertropia. The most common cause of presentation was cosmetic concern followed by diplopia. Two thirds of cases (80 patients) were non paralytic with neglected strabismus during childhood. Paralytic strabismus due to variable causes such as ischemia and trauma was seen in 32 patients. Surgery was done in 53 patients (44.2%). Six patients developed diplopia after surgery. In five of those the diplopia was temporary.

Conclusion: The majority of strabismus surgery in adults are cases neglected from childhood. The main indication for surgery was cosmetic. The outcome of surgery is excellent with rare occurrence of postoperative diplopia.

Ismat Ereifej

Correspondence:

Ismat Ereifej, MD
Senior Ophthalmology Consultant
Department of Ophthalmology at Royal Medical Services
Jordan

Email: ismat.ereifej@yahoo.com

Introduction

Strabismus is a common problem in childhood affecting 4% of children in the United States. In adults, one person among 100 suffers from strabismus (1-2). Common causes of strabismus in childhood include infantile esotropia, accommodative esotropia, congenital exotropia, deprivational strabismus and strabismus secondary to neurological problems (3). Treatment is primarily directed towards affecting amblyopia before aiming to align the eyes together by surgery (4-6). In adulthood, the etiology is different. The majority of cases are non paralytic with neglected cases from childhood (7). Paralytic causes such as nerve palsies associated with medical illnesses and trauma are common (8-11). Other causes include restrictive strabismus such as in thyroid eye disease (12).

Diplopia is a special problem that usually occurs in adult patients with strabismus but not in children as children's brains usually suppress one image from one eye (6). Another problem of concern is the lack of stereopsis as depth perception requires properly aligned eyes.

Treatment options include treating the underlying cause such as removing cataract for sensory deprivational strabismus. Correcting refractive error and amblyopia treatment is mandatory for children before considering surgery (7). In adults, the aim of surgical treatment is usually cosmetic. Other aims include restoration of binocular single vision, eliminating diplopia and abnormal head posture.

The aim of the study was to investigate presentation, causes and outcome of strabismus cases in adulthood.

Patients and Methods

A prospective study was conducted at Queen Alia Hospital of the Royal Medical Services during the period between August 2010 and August 2012. One hundred and twenty strabismus patients attending the ophthalmology clinic aged over 14 years were enrolled in the study. Patients were asked about onset of strabismus and symptoms complained of. Ophthalmologic examination included Snellen's chart best corrected visual acuity, orthoptic assessment, anterior segment examination via slit lamp and posterior segment examination via +78 lens after mydriasis. Refraction was done for all patients. The type of treatment, whether medical or surgical, was recorded. Complications of surgery were also recorded.

Results

A total number of 120 patients were enrolled in the study with age range of 14 years to 78.5 years (mean 34.2 years). Male to female ratio was 1.1 to 1. Sixty six patients (55%) had exotropia, 36.7% had esotropia and 8.3% had hypertropia. Most common cause of presentation was cosmetic concern followed by diplopia. Other symptoms included fatigue, near vision problems and abnormal head posture. Two thirds of cases (80 patients) were non paralytic with neglected strabismus during childhood. Paralytic strabismus due to variable causes such as ischemia and trauma was seen in 32 patients (Table 1 - opposite page). Surgery was done in 53 patients (44.2%). Six patients developed diplopia after surgery. Five of the diplopia cases were temporary and resolved by 4 weeks after surgery. Only one patient had persistent intractable diplopia. All of these patients complained of diplopia when tested preoperatively with prisms. We did not encounter any post operative complication such as scleral perforation or infection.

Discussion

Strabismus differs from children than the clinical picture in adults', etiology, outcome and management. The main symptom in children is the presence of squinting eye. Adults usually present for cosmetic reasons in non paralytic strabismus that is usually neglected or inappropriately managed from childhood. Other presentations in adults include diplopia, which is common in paralytic strabismus with vascular etiologies being the most common cause such as cranial nerve palsies that occur in diabetes or hypertension (1). Diplopia usually does not occur in children as their brain usually suppresses the image from one eye (6). This does not only prevent diplopia but also affects depth perception and stereoacuity. In adulthood strabismus, diplopia is common especially the paralytic type. In our study 60% of patients presented with cosmetic considerations; about one fifth of patients complained of diplopia. Other symptoms were near vision problems and fatigue. Abnormal head posture was seen in 5 patients.

The most common type of strabismus we found was exotropia (55% of patients). Esotropia was seen in more than one third of patients and hypertropia in 8.3%. This pattern also differs from what is usually seen in children where esotropia is more common with infantile and accommodative esotropia being the commonest two causes (7). Two thirds of our patients had neglected strabismus from childhood. Slightly more than a quarter of our patients had paralytic strabismus with diabetic cranial nerve palsy being the most common cause. Other causes included hypertension, hyperlipidemia, stroke and trauma. Restrictive strabismus due to thyroid eye disease was seen in 8 patients.

In children, the aim of treatment is primarily to prevent amblyopia and restore good vision to enable the patient to gain stereopsis. Infantile esotropia usually indicates surgery to improve binocular vision and stereopsis while accommodative esotropia is usually corrected with spectacles (5, 7, 13). In our group, surgery was done in 53 patients (44.2%). Six patients developed diplopia after surgery. In five of them, diplopia was

temporary and resolved within 4 weeks after surgery. Only one patient had persistent intractable diplopia. Examining patients with prisms before surgery to see the likelihood appearance of diplopia may identify some patients who have risk of postoperative diplopia (14-15). All of the six patients who complained of diplopia were tested preoperatively with prisms. Other post operative complications such as scleral perforation or infection were not seen in our series.

In conclusion, the majority of strabismus surgery in adults are neglected cases from childhood. The main indication for surgery was cosmetic. The outcome of surgery is excellent with rare occurrence of postoperative diplopia.

References

- Holgado S. Diplopia after strabismus surgery. *Am Orthopt J.* 2012; 62:5-8.
- Helveston EM. The value of strabismus surgery. *Ophthalmic Surg.* 1990; 21: 311-317.
- Fazzi E, Signorini SG, LA Piana R, Bertone C, Misefari W, Galli J, Balottin U, et al. Neuro-ophthalmological disorders in cerebral palsy: ophthalmological, oculomotor, and visual aspects. *Dev Med Child Neurol.* 2012; 54: 730-736.
- Kampanartsanyakorn S, Surachatkumtonekul T, Dulayajinda D, Jumroendarasmee M, Tongsaee S. The outcomes of horizontal strabismus surgery and influencing factors of the surgical success. *J Med Assoc Thai.* 2005; 88: 94-99.
- Baroncelli L, Maffei L, Sale A. New perspectives in amblyopia therapy on adults: a critical role for the excitatory/inhibitory balance. *Front Cell Neurosci.* 2011; 5: 25.
- Polat U. Restoration of underdeveloped cortical functions: evidence from treatment of adult amblyopia. *Restor Neurol Neurosci.* 2008; 26: 413-424.
- Caca I, Cingu AK, Sahin A, Ari S, Dursun ME, Dag U, Balsak S, et al. Amblyopia and Refractive Errors Among School-Aged Children With Low Socioeconomic Status in Southeastern Turkey. *J Pediatr Ophthalmol Strabismus.* 2012; 11:1-7.
- Bennett JL, Pelak VS. Palsies of the third, fourth, and sixth cranial nerves. *Ophthalmol Clin North Am.* 2001; 14: 169-185.
- Prasad S, Volpe NJ. Paralytic strabismus: third, fourth, and sixth nerve palsy. *Neurol Clin.* 2010; 28: 803-833.
- Schiavi C. Paralytic strabismus. *Curr Opin Ophthalmol.* 2000; 11: 318-323.
- Flanders M, Hasan J, Al-Mujaini A. Partial third cranial nerve palsy: clinical characteristics and surgical management. *Can J Ophthalmol.* 2012; 47: 321-325.
- Holmes JM, Hatt SR, Bradley EA. Identifying masked superior oblique involvement in thyroid eye disease to avoid postoperative A-pattern exotropia and intorsion. *J AAPOS.* 2012; 16: 280-285.
- Wutthiphan S. Guidelines for prescribing optical correction in children. *J Med Assoc Thai.* 2005;88: 163-169.
- Gunton KB, Brown A. Prism use in adult diplopia. *Curr Opin Ophthalmol.* 2012; 23: 400-404.

	Feature	Number of patients	Percentage
Type	Exotropia	66	55%
	Esotropia	44	36.7%
	Hypertropia	10	8.3%
Presentation	Cosmetic	72	60%
	Diplopia	23	19.2%
	Near vision problem	11	9.2%
	Fatigue	9	7.5%
	Abnormal head posture	5	4.2%
Cause	Non paralytic	80	66.7%
	Paralytic	32	26.7%
	Restrictive	8	6.7%

Table 1: Type, presentation and cause of strabismus

15. Flanders M, Sarkis N. Fresnel membrane prisms: clinical experience. *Can J Ophthalmol.* 1999; 34: 335-340.

Screening for chromosomal abnormalities by maternal age and fetal nuchal translucency thickness: The Jordanian experience

ABSTRACT

Objective: To screen for chromosomal defects on the basis of maternal age and fetal nuchal translucency thickness at 10 to 14 weeks of gestation.

Method: Fetal nuchal translucency thickness was measured by ultrasound examination at 10-14 weeks of gestation in living singleton pregnancies in women attending routine antenatal care at Prince Ali Bin Hussein, Amman Jordan.

The risks for trisomy 21 and other chromosomal defects by ultrasound measurement of fetal nuchal translucency thickness and maternal age were calculated, using the software provided by The Fetal Medicine Foundation.

Results: Chromosomal defects were diagnosed in 10 cases, including 4 cases of trisomy 21 and 6 cases with other chromosomal abnormalities (trisomy 18, 13, triploidy, Turner). The estimated risk based on maternal age and fetal NT was 1 in 300.

Conclusion: The combination of maternal age and fetal nuchal translucency thickness was an effective method of screening for chromosomal defects.

Keywords: Chromosomal abnormalities. Nuchal translucency. First trimester screening. Trisomy 21. Ultrasound.

Vera N. Amarin
Hussein M. Alsaied
Hussein h. Dmour
Fatmeh Al Quran

Correspondence:

Vera N. Amarin, MD
Department of Obstetrics & Gynaecology, Prince Ali Military Hospital, Karak Jordan
Department of Obstetrics and Gynaecology, Queen Alia Military Hospital, Amman Jordan
P. O. Box 850576
Amman 11181 JORDAN
Email: baceel@hotmail.com

Introduction

Increased fetal nuchal translucency (NT) thickness at 10-14 weeks is associated with chromosomal defects, cardiac anomalies and a wide range of genetic syndromes (1- 4).

The success of screening by fetal NT depends on the appropriate training of sonographers and the use of strict sonographic criteria including a good sagittal section with the fetus in the neutral position, with magnification such that the fetus occupies at least 75% of the image. Fetal skin should be distinguished from the amnion, and calipers used to measure the maximum thickness of the subcutaneous translucency between the skin and the soft tissue overlying the cervical spine (5, 6)

In our study, we used the approach advocated by The Fetal Medicine Foundation (FMF), which has coordinated a multicenter study involving 96,127 pregnancies. Screening by a combination of maternal age and fetal NT at a cut-off risk of 1 in 300 resulted in a sensitivity for the detection of trisomy 21 of 82% and a false-positive rate of 8% (7).

Methods

The study was conducted at Prince Ali Bin Al-Hussein Military Hospital, and Queen Alia Military Hospital over a 9-month period from 2007-2008. Women attending for routine antenatal care were offered ultrasound screening for fetal nuchal translucency (NT) at 10-14 weeks of gestation.

Using the software of the Fetal Medicine Foundation (FMF), the ultrasound scans were carried out by sonographers who have obtained the Fetal Medicine Foundation (FMF) certificate of competence in the theory and practice of the 10-14 week scan.

Fetal nuchal translucency (NT) was measured according to the guidelines recommended by the Fetal Medicine Foundation (FMF).

The necessary view requires that the fetal Crown-rump length (CRL) is between 38 mm and 84 mm, a good sagittal section of the fetus is used, the magnification of the image is such that the fetus occupies at least 75% of the screen, care is taken to distinguish between fetal skin and amnion, the maximum thickness of the subcutaneous translucency between the skin and the soft tissue overlying the cervical spine is measured with calipers placed on the lines (representing the nuchal skin and the underlying soft tissue).

At least three measurements were taken during the scan and the largest was recorded.

The scans were performed transabdominally unless visualization was poor, in which case vaginal sonography was used. On the basis of maternal age, fetal nuchal translucency (NT) and Crown-rump length (CRL) a risk for trisomy 21 is calculated using the FMF software. Patients with an estimated risk of 1 in 300 or more were offered fetal karyotyping by amniocentesis using both a direct method Interphase Fluorescence in situ Hybridization (FISH) and formal cell culture at the laboratory of medical genetics at King Hussein Medical Centre.

Patients with major fetal anatomical defects were excluded from the study. Demographic details and ultrasound findings, including, crown-rump length and nuchal translucency (NT)

were entered into an anonymized computer database at the time of scanning. Karyotype results and pregnancy outcome details were added as soon as these became available.

The fetal Crown-rump length (CRL) and nuchal translucency (NT) thickness were successfully measured in all cases.

Results

During the study period, the total number of pregnancies that presented at 10-14 weeks of gestation was 1,312. All were offered ultrasound measurement of the nuchal translucency. Fetal NT was successfully measured. The median maternal age was 28 years range 16-45 years as shown in Figure 1. The median gestational age was 12 weeks range 10-14.

The following patients were excluded from the study:

- A) 22 women presented too early in pregnancy.
- B) 416 too late in pregnancy.
- C) 21 presented with missed abortion
- D) 26 with twin pregnancy.

The numbers of alive singletons examined were 827 (Table 1 - next page). Antenatal karyotyping was performed by amniocentesis in 51 pregnancies because of an increased risk of aneuploidy, (>1 in 300) based on screening test (Table 2).

Maternal Age Distribution

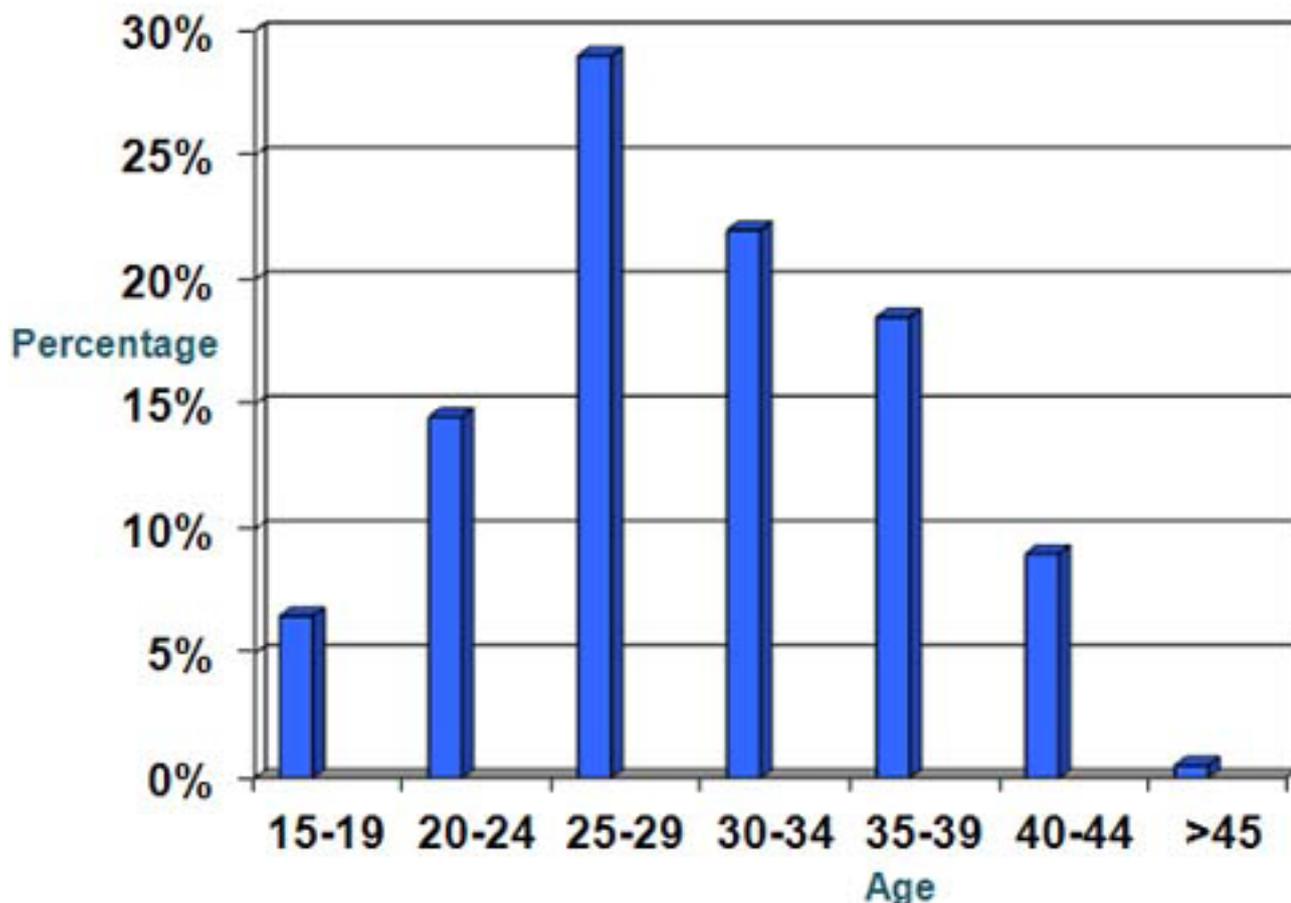


Figure 1: Maternal age distribution in the study group

	N	%
Total number of pregnancies	1312	100
Presented too late	416	31.7
Presented too early	22	1.7
Missed Abortion	21	1.6
Twins	26	2
Alive Singletons examined	827	63

Table 1: The number of alive singletons examined from the total number of pregnancies

Group	Total	Abnormal	Trisomy 21
Age ≥35 NT≥ 3mm	37	4	3
Age ≥35 NT <3mm	194	0	0
Age < 35 NT≥ 3 mm	14	2	1
Age < 35 NT< 3mm	582	0	0
Total	827	6	4

Table 2: Incidence of chromosomal abnormalities in relation to maternal age and increased NT

1	22 y	3.1mm	Tr 13	Amn 16	20 weeks	SM
2	26 y	4mm	Tr 18	Amn 16	32 weeks	IUD
3	35 y	3mm	Tr 21	Amn 16	38 weeks	Alive
4	36 y	5mm	Tr 18	Amn 16	20 weeks	SM
5	34 y	6mm	Tr 21	Amn 16	38 weeks	Alive
6	37 y	7mm	Tr 21	Amn 16	37 weeks	IUD
7	38y	8mm	Tr 21	Amn 16	20 weeks	SM
8	41y	5mm	45 x	Amn 16	33 weeks	IUD
9	43y	7mm	Tr18	Amn 16	30 weeks	IUD
10	46y	3mm	45 x	Amn 16	37weeks	NND

AMN=amniocentesis.

IUD=intrauterine death.

SM-spontaneous miscarriage.

NND-neonatal death.

Table 3: Pregnancy outcome in 10 chromosomal abnormalities in relation to maternal age and nuchal thickness examined at 10 to 14 weeks gestation

Chromosomal defects were diagnosed in 10 of these 51 pregnancies, including 4 cases of trisomy 21 (Table 3). In all cases of trisomy 21, the diagnosis was made prenatally but the option of termination is prohibited in Jordan. There were two live births, one intrauterine death and one spontaneous miscarriage.

There were 6 with other chromosomal defects, including 3 cases of trisomy 18, 1 of trisomy 13, 2 of Turner's syndrome (Table 3).

Discussion

The ultrasound screening test of (NT) was developed by Nicolaides K.H.(1) Currently, there are a number of studies examining this screening tool including 100,000 patients that give sensitivities between 70% and 90%, with a 4.3% false-positive rate (8,9).

Our results demonstrated the high acceptability of NT screening and the ability to obtain a measurement in all cases.

In our study, the median maternal age was 28 years and screening by a combination of maternal age and fetal NT identified approximately 90% of all major chromosomal defects for a false-positive rate of 5%.

These results in our population in Jordan were very similar to those obtained by the multicenter study of the FMF in Britain(2)

The findings confirm our suggestion that the methodology for measurement of fetal NT should be unified and provide further evidence for the lack of significant ethnic differences in fetal NT (10-13). Similar results were also obtained in a study in Greece with 3,550 pregnancies; the estimated risk was 1 in 300 or more in 4.9% of the population and this group contained 10 of the 11 (91%) fetuses with trisomy 21(14).

Our findings confirm that successful screening for chromosomal defects by fetal NT requires appropriate training of sonographers and that the same criteria needs to be used to achieve uniformity of results among different operators. However we prefer a large number of cases in future studies in order to reach a definite conclusion.

Conclusion

With the new millennium, there have been and probably will continue to be, major changes in the indications for invasive genetic testing, such that advanced maternal age alone will no longer be an indication.

In the future, the decision of whether a patient is at risk for fetal aneuploidy will be based on the combination of maternal age, multiple biochemical serum markers, and a complete ultrasound evaluation of the fetus.

Perhaps using this combined method, with appropriate training, high motivation and adherence to a standard technique for the measurement of NT we will be able to detect 90% of fetuses with chromosomal abnormalities while recommending amniocentesis to only 5% - 10% of pregnant women.

References

1. Nicolaides KH, Azar G, Byrne D, Mansur C, Marks K. Fetal nuchal translucency: ultrasound screening for chromosomal defects in first trimester of pregnancy. *BMJ* 1992; 304: 867-9.
2. Malone FD, D Alton ME, Berkowitz RL, Canick JA. First trimester screening for aneuploidy by nuchal translucency. *Am J Obstet Gynecol* 2000; 183: 1591-2.
3. Hyett J, Perdu M, Sharland G, Snijders R, Nicolaides KH. Using fetal nuchal translucency to screen for major congenital cardiac defects at 10-14 weeks of gestation: population based cohort study. *BMJ* 1999; 318: 81-54.
4. Souka AP, Krampfl E, Bakalis S, Heath V, Nicolaides KH. Outcome of pregnancy in chromosomally normal fetuses with increased nuchal translucency in the first trimester. *Ultrasound Obstet Gynecol* 2001; 18: 17.
5. Nicolaides KH, Brizot ML, Snijders RJM. Fetal nuchal translucency: ultrasound screening for fetal trisomy in the first trimester of pregnancy. *Br J Obstet Gynaecol* 1994; 101: 782-6.
6. Pandya PP, Snijders RJ, Johnson SP, Brizot ML, Nicolaides KH. Screening for fetal trisomies by maternal age and fetal nuchal translucency thickness at 10-14 weeks of gestation. *Br J Obstet Gynaecol* 1995; 102: 957-62.
7. Snijders RJ, Noble P, Sebire N, Souka A, Nicolaides KH. UK multicentre project on assessment of risk of trisomy 21 by maternal age and fetal nuchal translucency thickness at 10-14 weeks of gestation. Fetal Medicine Foundation First Trimester Screening Group. *Lancet* 1998; 352: 343-6.
8. Federico P, Shanthi S, Amarnath B, Baskaran T. First-trimester nuchal translucency, nasal bones, and trisomy 21 in selected and unselected populations. *Am J Obstet Gynecol* (2006) 194, 828-33.
9. Bindra R., Heath V., Liao A., Spencer K., Nicolaides K.H., One stop clinic for assessment of risk for trisomy 21 at 11-14 weeks: a prospective study of 15,030 pregnancies. *Ultrasound Obstet Gynecol* (2002) 20: pp 219-225.
10. Thilaganathan B, Khare M, Williams B, Wathen NC. Influence of ethnic origin on nuchal translucency screening for Down's syndrome. *Ultrasound Obstet Gynecol* 1998; 12: 112-4.
11. Jou HJ, Wu SC, Li TC, Hsu HC, Tzeng CY, Hsieh FJ. Relationship between fetal nuchal translucency and crown rump length in an Asian population. *Ultrasound Obstet Gynecol* 2001; 17: 111-4.
12. Strah DM. Risk assessment of trisomy 21 by maternal age and fetal nuchal translucency thickness in 7,096 unselected pregnancies in Slovenia. *J Perinat Med* - 01-JAN-2008; 36(2): 145-50.

13. Valerie J. Rappaport, MD. Prenatal Diagnosis and Genetic Screening Integration into Prenatal Care. *Obstetrics and Gynecology Clinics* - (September 2008); 35(3).
14. Theodoropoulos P, Lolis D, Papageorgiou C, Papaioannou S, Plachouras N, Makrydimas G. Evaluation of first-trimester screening by fetal nuchal translucency and maternal age. *Prenat Diagn* 1998; 18: 133-7

The Evaluation of the Patients Admitted With Hypoglycemia in an Emergency Department: From the Perspective of an Emergency Specialist

ABSTRACT

Objective: Hypoglycemic disorders are very common in emergency settings. They are generally seen in diabetic patients with under-treatment. The case should be urgently treated after a differential diagnosis. In this retrospective study, our aim is to investigate the etiology of hypoglycemia in the patients admitted to the emergency department.

Material and Methods: This study was carried out during 2008 at the Department of Emergency Medicine (EM) in a Training and Research Hospital, and 5,000 consecutive patients admitted to EM were enrolled. They were evaluated in aspects of hypoglycemia by clinical and biochemical investigation.

Results: Of these patients, 35 of them (female 16, male 19) were diagnosed as having hypoglycemia. The mean plasma glucose level was 38.7 ± 10.6 mg/dL. The most common cause of hypoglycemia is due to inappropriate diabetic drug usage in 32 (91%) cases with diabetes mellitus (DM), and most of them 24 (68%) were insulin using diabetic patients. The other three (9%) patients had the diagnosis of chronic renal failure, and Sheehan syndrome, respectively. However, the etiology of hypoglycemia was not found in the third case.

Conclusion: It was found that the prevalence of hypoglycemia was approximately 0.7% in patients with DM admitted to EM. Insulin and/or oral antidiabetic treatment in cases with DM were the most important etiology in aspects of hypoglycemia. The causes of this disorder can change according to countries. The diminished prevalence of hypoglycemia in comparison to the previous reports may be due to qualified patient education and management such as glucometer and insulin pumps.

Key words: Diabetes mellitus, hypoglycemia, emergency department

Huseyin Cebicci (1)
Ali Karakus (2)
Cumali Gokce (3)
Sedat Motor (4)
Cem Zeren (5)
Murat Yucel (1)
Nurullah Gunay (1)
Rami Helvacı (3)

(1) Kayseri Training and Research Hospital, Department of Emergency Medicine, Kayseri, Turkey
(2) Mustafa Kemal University Medical Faculty, Department of Emergency Medicine, Hatay, Turkey
(3) Mustafa Kemal University Medical Faculty, Department of Internal Medicine, Hatay, Turkey
(4) Mustafa Kemal University Medical Faculty, Department of Biochemistry, Hatay, Turkey
(5) Mustafa Kemal University Medical Faculty, Department of Forensic Medicine, Hatay, Turkey

Correspondence:

Ali Karakus, Assistant Professor
Mustafa Kemal University
School of Medicine
Department of Emergency Medicine
Hatay, Turkey
Phone: 03262291000
Fax: 03262455654
Email: drkarakus@yahoo.com

Introduction

Hypoglycemia is the most frequent endocrine emergency and easily treatable condition in pre-hospital and emergency department settings (1-5). The disorder causes substantial clinical impact in terms of mortality, morbidity, and quality of life (6).

Hypoglycemia is defined as the incidence of a wide variety of symptoms followed by plasma glucose concentration of 50 mg/dL (2.8 mmol/L) or less (7). It is common knowledge that many drugs, endocrine-related disorders, malignancies, malnutrition, and renal insufficiency can cause hypoglycemia. The agents used in Diabetes Mellitus (DM) treatment are the most common drugs for the etiology of hypoglycemia (2,3,8).

Hypoglycemia in patients with DM is often unnoticed where there is a diabetic neuropathy resulting in patients' losing their ability to sense hypoglycemia (unawareness of hypoglycemia) over time, which increases their risk in terms of cardiovascular morbidity and mortality (9,10). The aim of the present study is to investigate the prevalence and the causes of hypoglycemia in patients with DM admitted to the hospital's emergency clinic.

Material and Methods

This study was carried out during 2008 at the Department of Emergency Medicine (EM) in a Training and Research Hospital. We defined hypoglycemia by plasma glucose concentration of 50 mg/dL (2.8 mmol/L) or less (7). In the Department, the glucose level was measured simultaneously by a glucometer in capillary blood and the glucose oxidize method in venous plasma in the laboratory. Therefore, the confirmation of the diagnosis was double checked in aspects of glucose assays. All the patients had Whipple triads in terms of the diagnosis. Patient files were recorded for multiple variables including age, sex, glucose levels, renal and liver function test, determination of the etiology such as drugs, hypocortisolemia (10). Laboratory analyses of the samples were done immediately. Chronic renal failure was diagnosed as a glomerular filtration rate (GFR) below 60 mL/ min, and end-stage renal disease was diagnosed if the patient had a GFR lower than 10 mL/min or had renal replacement therapy (dialysis). Liver failure diagnosis was done related to clinical and laboratory assessment. All the undiagnosed cases in terms of etiology were consulted by an endocrinologist (CG).

Results

During the study period, 5,000 patients were admitted to the EM due to endocrine emergencies. Hypoglycemia was detected in 35 (0.7%) of the patients. All the patients except one were discharged from the hospital after treatment. An insulin using patient with DM was hospitalized due to extended hypoglycemia. Of these 35 patients, 16 were female, median age 61 years old (range 27-85 years). There were 19 males with a median age of 65 year-old (range 20-82 years). The mean glucose levels were 38.7±10.6 mg/dL. The etiologies of hypoglycemia are presented in the Table 1 - below. The most common etiology of hypoglycemia in patients with DM was inappropriate drug therapy (32: 91%) such as insulin and/or oral antidiabetics. One patient died due to hypoglycemia induced acute myocardial infarction.

Three (9%) patients were not previously diagnosed as DM. One of them had chronic renal failure. The second patient was diagnosed as Sheehan syndrome for 3 years, but she did not receive the medication for adrenal insufficiency and secondary hypothyroidism for one week. The case also had glucocorticoid and thyroid replacement therapy in addition to dextrose-saline infusion for the disorder. The third case was investigated for the differential diagnosis of hypoglycemia. However, the patient had no etiological diagnosis.

Discussion

It is well known that hypoglycemia is one of the most frequent endocrine emergencies in daily clinical practice (2-5). Early diagnosis of the disorder and determination of the underlying etiology are necessary for definitive diagnosis and management.

Spontaneous hypoglycemia in renal failure is more common than being considered. Hypoglycemia detections should be based on frequent and careful glucose determinations in patients with uremia (11,12). In a study, Fischer et al evaluated 137 hypoglycemic episodes occurring with 94 patients admitted with hypoglycemia to the hospital. Forty-six of all patients had chronic renal insufficiency, and 20 of these were due to DM (13). In our study, only one patient had chronic renal failure. This difference may be due to not including the hospitalized patients in the current report.

In our study, similar to other studies, the most common cause of hypoglycemia was due to inappropriate usage of antidiabetic agents. Of these drugs, hypoglycemia because of insulin therapy was the most common (68%), and hypoglycemia induced by oral antidiabetic agents was found as 23%.

The Etiology	Number	(%)
Diabetes mellitus	32	(91)
Insulin therapy	24	
Oral anti-diabetic agents	8	
Non-diabetics	3	(9)
Chronic renal failure	1	
Unknown	2	
Total	35	(100)

Table 1: The etiology of hypoglycemia in the patients with DM

Limited data is available on the etiology of hypoglycemia in patients admitted with the disorder. Gossel et al reported that drug induced hypoglycemia accounted for 56.3% cases of adverse drug reactions and included mainly patients on insulin with or without an oral antidiabetic agent. Many of these diabetic patients also had co-morbidities and were on multi-drug therapy (14).

Hypoglycemia is mostly seen in diabetic patients due to overdose of antidiabetic agents, low calorie intake, malnutrition, excessive exercise, prolonged starving, and development of either renal or hepatic failure (2,6,15,16). These values do not represent the real frequency of hypoglycemia among diabetic patients, which is much higher; the majority of such cases are home-treated due to the fact that patients and/or their relatives are well aware of the hypoglycemia symptoms (17).

One case previously had a diagnosis of panhypopituitarism due to Sheehan syndrome (SS) and she did not use her medications for the disorder. Therefore, she probably had hypoglycemia due to drug withdrawal. The causes of hypoglycemia seem to vary from one country to another. It was shown that SS was one of the important etiologies of hypoglycemia especially in developing countries (18).

However, a patient with hypoglycemia was not diagnosed in terms of etiology in spite of very detailed investigation. Mortality due to hypoglycemia was reported to change from 4% to 27% (13,19). We found a mortality rate of 2.85 %, and it is due to acute myocardial infarction. All the patients were recommended for follow up in outpatient clinic controls in Endocrinology and Metabolism Department.

Conclusion

As a result, it was found that the prevalence of hypoglycemia was approximately 0.7% in patients with DM admitted to EM. Insulin and/or oral antidiabetic treatment in patients with DM were the most important etiology in aspects of hypoglycemia. The causes of this disorder can change according to countries. The diminished prevalence of hypoglycemia in comparison to the previous reports may be due to qualified patient education and management such as glucometer and insulin pumps. Emergency physicians should set the early diagnosis of hypoglycemia in order not to expose malpractice.

References

1. Yealy DM, Wolfson AB. Hypoglycemia. *Emerg Med Clin North Am* 1989;7:837-48.
2. Soltész G. Hypoglycaemia in the diabetic child. *Baillieres Clin Endocrinol Metab* 1993;7:741-55.
3. Vignesh JP, Mohan V. Hypoglycaemia unawareness. *J Assoc Physicians India* 2004;52:727-2.
4. Comi RJ. Approach to acute hypoglycemia. *Endocrinol Metab Clin North Am* 1993;22:247-62.
5. Service FJ. Hypoglycemia. *Med Clin North Am* 1995;79:1-8.
6. Amiel SA, Dixon T, Mann R, Jameson K. Hypoglycaemia in Type 2 diabetes. *Epub* 2008;25:245-54.
7. Field JB. Hypoglycemia. Definition, clinical presentations, classification, and laboratory tests. *Endocrinol Metab Clin North Am* 1989;18:27-43.
8. Meijer E, Hoekstra JB, Erkelens DW. Hypoglycaemia unawareness. *Presse Med* 1994;23:623-7.
9. Gabriely I, Shamon H. Hypoglycemia in diabetes: common, often unrecognized. *Cleve Clin J Med* 2004;71(4):335-42.
10. Kahn C.R. , Weir GC., King GL., Jacobson AM., *JOSLIN'S Diabetes Mellitus Fourteenth Edition, Hypoglycemia*, Glaser B and Leibowitz G.,MA 02215, Chapter 69, By Joslin Diabetes Center One Joslin Place Boston 2005: 1147-75.
11. Arem R. Hypoglycemia associated with renal failure. *Endocrinol Metab Clin North Am* 1989;18:103-21.
12. Fiorini F, Raffa M, Patrone E, Castelluccio A. Glucose metabolism and chronic renal insufficiency. *Arch Ital Urol Androl* 1994;66:51-6.
13. Fischer KF, Lees JA, Newman JH. Hypoglycemia in hospitalized patients. *N Engl J Med* 1986;315:1245-50.
14. Gossell-Williams M, Williams-Johnson J, Francis L. Hypoglycemic complications with diabetes mellitus management: the predominant adverse drug reaction presenting to the Accident and Emergency Department of The University Hospital of the West Indies. *West Indian Med J* 2010;59:555-60.
15. Cryer PE, Binder C, Bolli GB, et al. Diabetes. Hypoglycemia in IDDM. *Diabetes* 1989;38:1193-9.
16. Lheureux PE, Zahir S, Penaloza A, Gris M. Bench-to-bedside review: Antidotal treatment of sulfonylurea-induced hypoglycaemia with octreotide. *Diabet Med*. 2008 1: Crit Care 2005;9:543-9.
17. Cryer PE, Davis SN, Shamon H. *Diabetes Care*. Hypoglycemia in diabetes 2003;26:1902-12.
18. M Güven, F, Bayram, K Güven, F Kelestimur. Evaluation of patients admitted with hypoglycaemia to a teaching hospital in Central Anatolia *Postgrad. Med. J* 2000;76:150-2.
19. Nouel O, Bernuau J, Rueff B, Benhamou JP. Hypoglycemia: a common complication of septicemia in cirrhosis. *Arch Intern Med* 1981;141:1477-8.

Primary Lymphoma of the Uterine Cervix: A Case Report

ABSTRACT

Primary non-Hodgkin's lymphoma (NHL) of the uterine cervix is an exceedingly rare entity and often poses a diagnostic challenge if its existence is not suspected.

We herein report a case of primary uterine cervix NHL with an unusual presentation as urine retention. Despite typical local manifestation of the genital tract primary NHLs, the uncommon site of this entity may lead to misdiagnosis by pathologists and clinicians who are unfamiliar with their clinical and pathologic features.

Because of the low incidence of primary genital tract lymphomas there are no universal protocols regarding treatment. Our patient received multiple courses of chemotherapy and has remained disease free more than a year from the time of diagnosis.

We concluded that chemotherapy with the Cyclophosphamide, Adriamycin, Oncovin, Methotrexate and prednisolone protocol is an effective and tolerable treatment option.

Multicenter well-controlled studies and analysis of case reports are necessary to evaluate the long-term results of different chemotherapy protocols in the treatment of these primary NHLs of the genital tract.

Keywords: Uterine cervix non-Hodgkin's lymphoma, genital tract, urine retention, large B-cell lymphoma.

Mohammad Al Quddah

Correspondence:

Dr. Mohammad Al Quddah, Consultant Obs & Gyn,
Royal Medical Services (RMS),
Jordan
Mobile 962795558890
Email: mawadqudah@yahoo.co.uk

Introduction

The female genital tract is a rare site of Primary NHLs, and only a few cases of primary lymphomas involving the uterine cervix have been reported. In fact, only 1.5% of extranodal lymphomas originate in the female genital tract; the uterine cervix appears to be the least often involved and the ovary being the most commonly affected site (1). Primary lymphomas of the female genital tract are mostly present as non-Hodgkin's lymphoma (NHL) of diffuse large B-cell histologic type (2). These lymphomas may involve the gynecologic tract, most often as a manifestation of systemic disease (3).

Although uncommon, lymphoma should be included in the differential diagnosis of gynecologic malignancies because of a usually favorable outcome when properly diagnosed and treated (4). Histologic examination and careful morphologic evaluation of obvious lymphoid components are warranted to make the correct diagnosis and to pursue the appropriate staging and therapeutic decision in case of malignant lymphoma (5).

Case Presentation

A 49-year old, Para 6, postmenopausal women with a past medical history of hypertension and diabetes presented with postcoital bleeding and urine retention. She also complained of increased vaginal discharge during the last three months. There was no history of fever, weight loss or night sweats.

Physical examination was unremarkable. Pelvic examination, however, revealed a bulky and barrel-shaped cervix with bleeding on touch at the anterior lip. The cervix was firm and nodular in consistency. The upper third of the anterior vaginal wall was thick and hard.

Hematological investigation revealed microcytic hypochromic anemia. Liver and kidney functions tests were all within normal limits. Papanicolaou smear was normal. Ultrasound scan of the pelvis revealed an enlarged cervix measuring 5.5 x 7.5 centimeters in diameters.

Based on her clinical history and local physical examination, a provisional diagnosis of cervical malignant tumor (mostly lymphoma) was made.

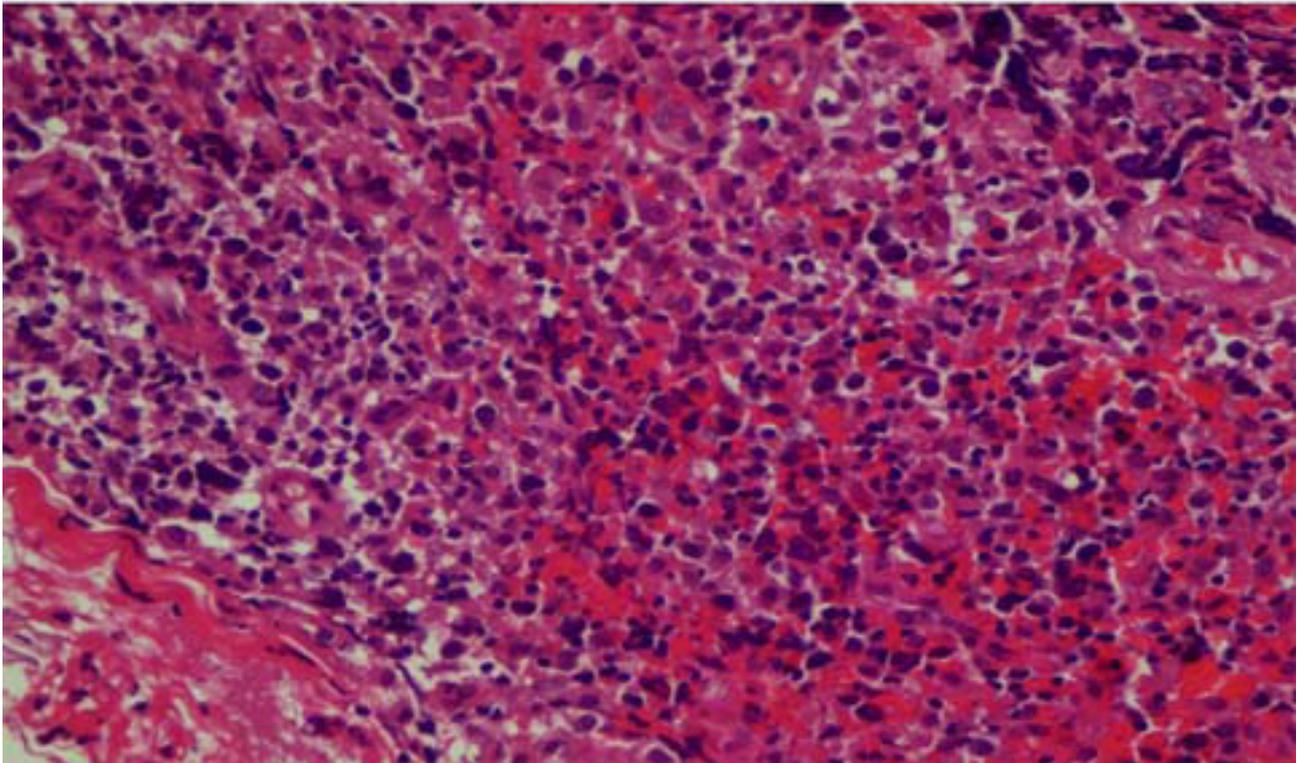


Figure 1: Diffuse large B-cell cervical lymphoma



Figure 2: A computerized tomography of the abdomen and pelvis revealed a 8x7.5 centimeters mixed density mass lesion seen posterior to bladder

She was then listed for examination under anesthesia, for punch cervical biopsy and hysteroscopy with endometrial biopsy. The histology of the cervical biopsy was reported initially as polypoidal granulation tissue with no definite evidence of malignancy and if there is a clinical suspicion of malignancy another biopsy is advised. The hysteroscopic and the endometrial histologic findings were unremarkable with no evidence of hyperplasia or malignancy.

The punch cervical biopsy was repeated and the histologic examination reported as diffuse large B-cell cervical lymphoma (Figure 1). The vaginal biopsy revealed unremarkable vaginal tissue. Subsequently the immunohistochemical analysis showed an evidence of massive positivity to CD-45 and B-cell markers including CD-20.

A computerized tomography of the abdomen and pelvis revealed a 8 x 7.5 centimeters mixed density mass lesion seen posterior to bladder invading the bladder base with severe left and mild right hydronephrosis, multiple enlarged iliac and pelvic lymph nodes, the largest measuring 5 centimeters in diameter and omental thickening and intra-abdominal ascites were noted. There were also multiple hypodense lesions in the right lobe of the liver (Figure 2).

Pelvic MRI revealed a 7 x 7.5 centimeters mass lesion in the uterine cervix. The mass appears to invade the urinary bladder posteriorly. Bilateral iliac lymph nodes were noted. These findings are suggestive of cervical malignant tumor (Figure 3 and 4).

Six cycles of chemoimmunotherapy (Cytoxan, Adriamycin, oncovin, mabthera and prednisolone) were administered. Complete remission was achieved after six cycles according to the restaging CT and MRI. The patient was disease free during the next 12 months.

Discussion

Lymphomas of the female genital tract are uncommon; primary NHLs are still rarer. A review of the literature shows that 1 in 175 extranodal lymphomas in females is likely to originate in the vagina, uterus or cervix (6). The age at presentation ranges from 20-80 years, with the median age varying from 40-59 years (7).

Abnormal vaginal bleeding is the most common presenting symptom of malignant lymphoma of the uterine cervix (8). Our patient presented with postcoital bleeding and urine retention. The Papanicolaou smear was negative. This case serves to take into consideration the possibility of uterine cervix involvement with a primary malignant lymphoma. The findings on cervical cytology in these women with lymphomas are variable. In most cases (as in our case) the cervical smear is negative, which is most likely due to the fact that these lymphomas invade the cervical stroma, and squamous and glandular epithelial lining is initially preserved. Positive findings on cervical cytology may result if there is ulceration. A deep cervical excisional biopsy may give a definite diagnosis (9).

Clonality testing is now a standard tool that is used in some cases of suspected lymphoproliferation. The biomed-2 approach is now commonly seen as the most optimal approach (10). There is an evidence that genital tract NHLs may be under-diagnosed by pathologists who are unfamiliar with their clinical and pathologic features, both because these tumors are unlikely to occur in these sites and because they may be misdiagnosed as either inflammatory lesions or as other types of malignant tumors (11).

Diagnosis of such rare tumors requires a high degree of clinical suspicion when the histologic specimen seems atypical of a chronic lymphocytic cervicitis, primary squamous cell or adenocarcinoma of the cervix (12), which can be confused with a primary lymphoma.

The pathogenesis of cervical NHL is unclear and they are usually classified in MALT-oma category (mucosa-associated lymphoid tissue) because of relatively low malignancy, good prognosis and localized growth (13). The diagnostic evaluation of cervical tumors should include computerized tomography (CT) or magnetic resonance imaging (MRI) of the pelvis and abdomen to determine lymph node status. Cervical NHL can occasionally be differentiated from cervical carcinoma by means of MRI of the mucosa, as well as sparing of the cervical stroma and the uterine junctional zone, are the most important findings to distinguish cervical lymphoma from carcinoma, and are best evaluated with T2 turbo spin echo sequence. Post-contrast images help to delineate the extent of the disease (14).

The prognosis of cervical lymphoma is good, even with local spreading and advancement of the tumor at the time of presentation. Extent of the disease, size of the tumor, and the histologic type of the lymphoma are the most important prognostic features of the disease, but because of its rarity, the standard treatment has not been established.

Treatment options for the NHLs of the female genital tract include surgery, chemotherapy and radiotherapy. As these tumors are usually diagnosed after surgery, the treatment options include chemotherapy with or without radiotherapy.

In cases diagnosed before surgery, primary external beam radiotherapy followed by brachytherapy; surgery followed by chemotherapy (16); and radiotherapy or neoadjuvant chemotherapy followed by surgery (17) have all been advocated depending on age of the patient, histologic type and stage of the tumor. There is no significant advantage of radical surgery in patients with cervical NHLs.

Conclusion

Cervical excisional biopsy followed by proper histologic examination by an experienced pathologist is essential to establish the correct diagnosis of cervical lymphoma.

Although a rare malignant tumor, NHL of the uterine cervix has a good prognosis with adequate treatment.

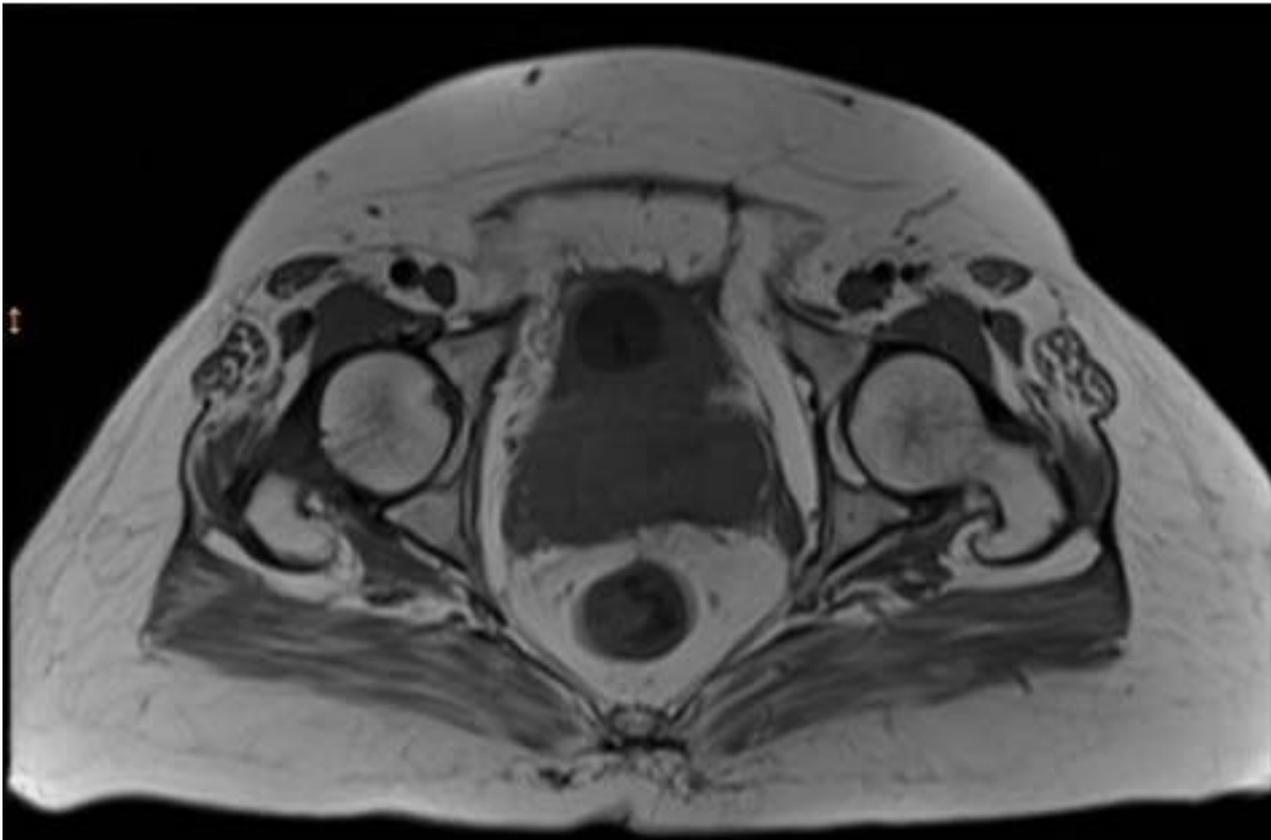


Figure 3: Pelvic MRI revealed a 7x7.5 centimeters mass lesion in the uterine cervix

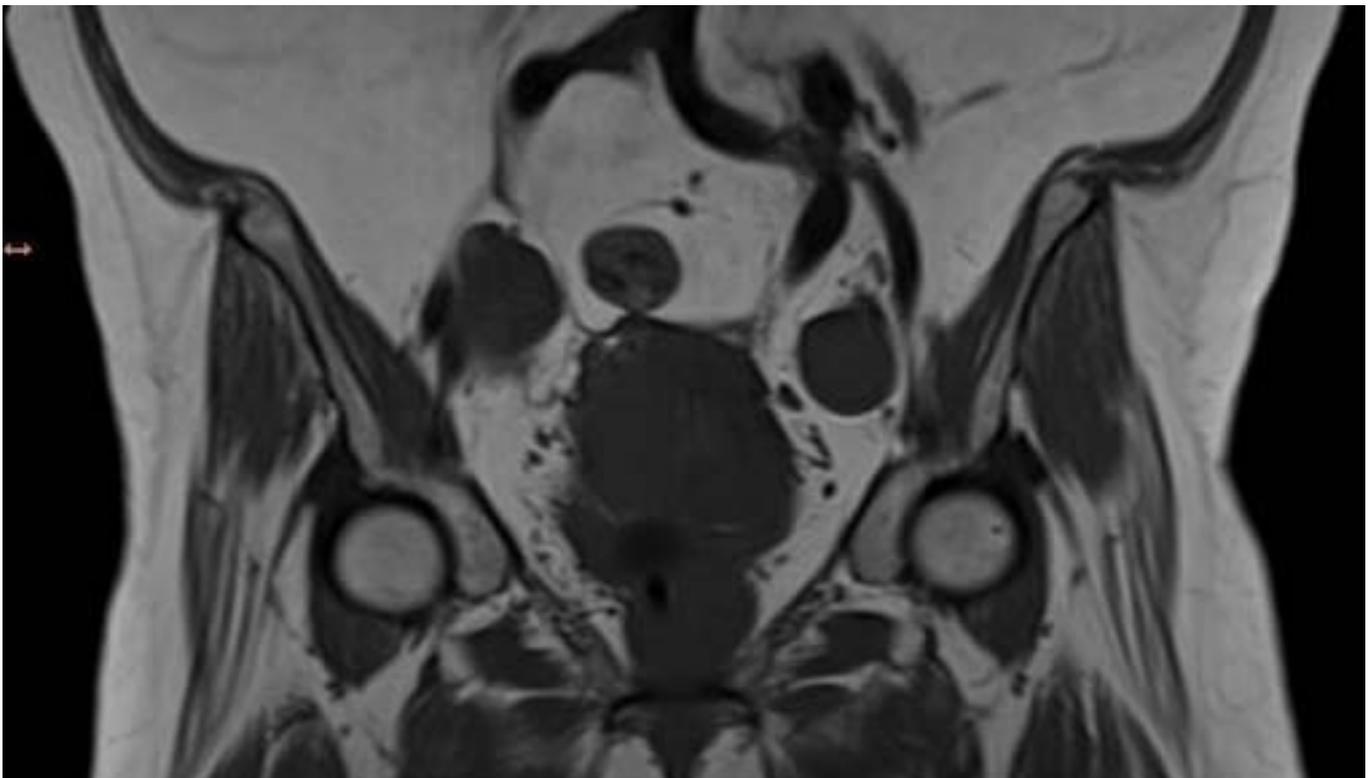


Figure 4: Pelvic MRI revealed a 7x7.5 centimeters mass lesion in the uterine cervix. The mass appears to invade the urinary bladder posteriorly. Bilateral iliac lymph nodes were noted

References

1. Frey NV, Svoboda J, Andreadis C, Tsai DE, Schuster SJ, Elstrom R. Primary lymphoma of the cervix and uterus. *Leuk Lymphoma* 2008; 47:1894-1901.
2. Young G. Lymphoma of uncommon sites. *HematolOncol* 1999; 17: 53-83.
3. Vang R, Mederious LJ, Malpica A. Non-Hodgkins Lymphoma involving the vulva. *Int J GynecolPathol* 2007; 19: 236-242.
4. Biljan SM, Maja DP, Ljubomin RJ. *Med Oncol* 2008; 25: 245-247.
5. Annibali O, Romeo AA, Agostinelli F, Marchesi A, Titindelli MC, Pileri SA. A case of primary MALT lymphoma of the endometrium presenting as asymptomatic polyp. *Ann Hematol* 2009; 88: 491-493.
6. Grace A, Connel N, Byrne P, Prendiville W, Donnell R, Roysron D, Walsh CB. Malignant Lymphoma of the cervix: an unusual presentation and a rare disease. *Eur J GynecolOncol* 1999; 20(1): 26-28.
7. Sobotkowski J, Blasinska M, Dowgier I. Vaginal bleeding as a first symptom of malignant lymphoma: case reports, diagnosis and successful treatment. *Eur J GynecolOncol* 2004; 25(2): 245-246.
8. Marin C, Seoane JM, Sancez M, Ruiz Y, Garcia JA. Magnetic resonance imaging of primary lymphoma of the cervix. *EurRadiol* 2010; 12(6): 1541-12280
9. King J, Elkhalfifa M, Michael C. Malignant lymphoma identified on cervical cytologic smear with immunophenotypic analysis. *ActaCytol* 2006; 40: 1228.
10. Patel KP, Pau Q, Wang Y, Maitta RW, Ratech H, Xue X. Comparison of BIOMED-2 versus laboratory-developed polymerase chain reaction assays for detecting cell receptor (gamma) gene rearrangement. *J MolDiag* 2010; 12: 266-267.
11. Kosari F, Daneshbod Y, Parwadesh R, et al. Lymphomas of the female genital tract: a study of 186 cases and review of the literature. *Am J SurgPathol* 2005; 29: 1512-20.
12. Stroth E, Besa P, Cox J, et al. Treatment of patients with lymphomas of the uterus or cervix with combination chemotherapy and radiation therapy. *Cancer J* 2006; 75: 2392-99.
13. Omari AH, Keadani T, Benjaafar N, Ghazi E, Gueddari BK. Non-Hodgkins lymphoma of the uterus: apropos of 4 cases and review of the literature. *Cancer Radiother* 2009; 6(1): 39-45.
14. Marin C, Seoan JM, Sanchez M, Ruiz Y, Carcia JA. Magnetic resonance imaging of primary lymphoma of the cervix. *EurRadiol* 2002; 12(6): 1541-45.
15. Muntz HG, Ferry JA, Flynn D, Fuller AF, Tarraza HM. Stages of primary malignant lymphomas of the uterine cervix. *Cancer* 2009; 68(9): 2023-32.
16. Bollerman C, Reuter T, Weber FW, Schwenzer T. Immunoplastic highly malignant lymphoma of the uterine cervix. *ZentrallbiGynakol* 1996; 118: 673-75.
17. Szanto A, Bellaga JJ, Csapo Z, Streter LL, Matolcsy A, Papp Z. Primary Non-Hodgkins lymphoma of the uterine cervix successfully treated by neoadjuvant chemotherapy: case report. *GynecolOncol* 2010; 89(1): 171-174.