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Garyounis Medical Journal (GMJ)

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Acknowledgements

Acknowledgements should he made only to those who have made a substantial contribution to the study. Authors are responsible for obtaining written permission from people acknowledged by name in case readers infer their endorsement of data and conclusions.

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2. *Organization as author*

The Cardiac Society of Australia and New Zealand. Clinical exercise stress testing. Safety and performance guidelines. Med J Aust 1996; 164: 282-4.

3. *No author given*

Cancer in South Africa [editorial]. S Afr Med J 1994;84:15.

4. Article not in English

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N.B. an English translation should be submitted.

5. *Volume with supplement*

Shen HM, Zhang QF. Risk assessment of nickel carcinogenicity and occupational lung cancer. Environ Health Perspect 1994;102 Suppl 1:275-82.

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Enzensberger W, Fischer PA. Metronome in Parkinson's disease [letter]. Lancet 1996;347:1337.

Clement J, De Bock R. Hematological complications of hantavirus nephropathy (HVN) [abstract]. Kidney Int 1992;42:1285.

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1. *Personal author(s)*

Ringsven MK, Bond D. Gerontology and leadership skills for nurses. 2nd ed. Albany (NY): Delmar Publishers; 1996.

2. *Editor(s), compiler(s) as author*

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4. *Conference proceedings*

Kimura J, Shibasaki H, editors. Recent advances in clinical neurophysiology. Proceedings of the 10th International Congress of EMG and Clinical Neurophysiology; 1995 Oct 15-19; Kyoto, Japan. Amsterdam: Elsevier; 1996.

5. *Dissertation*

Kaplan SJ. Post-hospital home health care: the elderly's access and utilization [dissertation]. St. Louis (MO): Washington Univ.; 1995.

6. *Dictionary and similar references*

Stedman's medical dictionary. 26th ed. Baltimore: Williams & Wilkins; 1995. Apraxia; p. 119-20.

Electronic Material

1. *Journal article in electronic format*
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2. *Monograph in electronic format*
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The Demographic Impact of AIDS On Future Mortality

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Department of Statistics, Faculty of Science, University of Garyounis; Benghazi; Libya.

الملخص

شهد العقد الماضي تهديدا متناميا للبشرية بانتشار مرض فقد المناعة وتلخص هذه المقالة المعلومات المتاحة الخاصة بتأثير وفيات مرض الإيدز علي اتجاه الوفيات ولفهم و تقيم هذا المرض علي الوفيات، توجد أربعة خصائص لهذا المرض يجب اعتبارها وأولها انه يتوجب علينا التسليم بان مرض الإيدز هو مرحلة متأخرة لمرض نقص المناعة و عليه فأن انتشار الميكروب هو النتيجة القاتلة، و ثانيا إن السبب الطبيعي لعدوي نقص المناعة تتسم بطول فترة الإصابة حيث إن الشخص الذي يبدو خاليا من المرض و لكنه يحمل ا لميكروب يمكن نقل هذا المرض جنسيا أو عن طريق العامل مع الدم، و ثالثا في حالة عدم التوصل إلي علاج شافي من هذا المرض في المستقبل القريب فان حوالي 50% من المصابين حاليا بمرض نقص المناعة سيدخلون في مرحلة مرض الإيدز خلال فترة 10-12 سنة، و رابعا عند مقارنة عدد المتوفين بأمراض أخري، نجد إن مرضي الإيدز يتوفون عند متوسط عمر حوالي 37 سنة، هذا بالنسبة لمرض الإيدز في بريطانيا. وصلت التقديرات العالمية 1997 بان الأشخاص الباقين علي قيد الحياة ومصابون بمرض فيروس العوز المناعي البشرى و مرض العوز المناعى حوالي 30.6 مليون وان المصابين الجدد بمرض فيروس العوز المناعى البشرى حوالي 5.8 مليون و إن الوفيات بسبب مرض العوز المناعى 2.3 مليون.

Abstract

Since 1981, when the first cases of AIDS were identified and diagnosed, HIV/AIDS has emerged as one leading challenges for global public health. Particularly in Sub-Saharan Africa, where of the majority of HIV/AIDS cases appear, the epidemic continues to take a massive human toll. By the end of 2002 more than 65 million persons had been infected by HIV, about 42 million were still alive, 38.6 million adults and 3.2 million children. According to (UNAIDS), AIDS has been the fourth most important cause of death in the world and it is already the leading cause of death in Sub-Saharan Africa (UNAIDS, 2001). The rapid spread of the disease has meant that in the most effected regions, there is an escalating demand for care by those infected. The detrimental impact of HIV/AIDS epidemic is also felt in developing countries, where 93% of those infected with HIV lived at the end of 2002, Sub-Saharan Africa with more than 29 million persons living with HIV at that date. The number of infected persons is rising in Asia and Latin America and the Caribbean. It is estimated that by the end of 2002 Asia had more than 7.0 million persons infected with HIV and an additional 1.9 million HIV-positive persons lived in Asia, Latin America and the Caribbean (UNAIDS/WHO 2002).

Key words: HIV, AIDS, Survival rate, YPPL

Introduction

It must be realized that AIDS is the last stage of an infectious disease, which is caused by human immunodeficiency virus (HIV). The spread of the virus and not the low number of AIDS cases and deaths which is the crucial factor. The natural course of an HIV infection is characterized by its incubation period in which the carrier can transmit the virus both sexually and through blood contact. If no cure is found in the near future, about 50% of all those presently infected with HIV will develop AIDS and die during the next 10 to 12 years. Compared to the victims of other causes of deaths, AIDS patients die young. The present average age at death is 37 years. The interaction between human immunodeficiency virus (HIV) and the immune system has a complex and postponed development. In a typical progression, the virus replicates rapidly during the first weeks or months following infection, then the immune response produces antibodies that reduce viral abundance, and HIV antigens may be undetectable during a long interval before the development of AIDS (Acquired Immunodeficiency Syndrome) takes place.

The past and future evolution of the HIV epidemic

The number of persons infected with HIV/AIDS is not evenly distributed over the main areas of the globe. 70% of HIV infected persons in 2001 were reported in the countries of sub-Saharan Africa, while only 11% of the world's population occupies this region. The levels of prevalence among adults aged 15-49 differs from one region to another. According to current estimates, the mean time elapse between the year of widespread transmission and the year of peak incidence is 13.8 years. The evolution of annual prevalence levels in the population aged 15-49 shows great variation among effected countries is evident in both the past and the future path of the epidemic.

1.1 The Natural History of HIV Infection and AIDS: to understand the impact of AIDS on future trends of mortality, it is essential to understand some medical

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facts about HIV infection. The natural course of this disease consists of several stages, which is graphed in figure 1 and described below.

a- ***Infection***: The disease starts when (HIV) invade certain human cells (T-helper-cells, macrophages, brain cells).

b- ***Initial lymphatic reaction:*** A short time after infection, some patients (10%-15%) suffer from fever like influenza.

c- ***A symptomatic latency period***: is the latency period between initial infection and the development of AIDS.

d- ***AIDS-related complex (ARC):*** This stage is reached after several years of HIV infection; normally ARC patients have a high probability of progressing to AIDS.

e- ***Full-blown AIDS:*** This is only the terminal stage of this infectious disease and not the disease itself.

Clinical research has demonstrated that the virus not only affects the human immunity system, but also responsible for the diversity of neurological syndromes including progressive dementia.

Demographic impact of HIV/ AIDS

The impact of AIDS may be assessed by considering the changes in demographic indicators brought about by the disease. Three sets of demographic indicators are examined

a- The overview of population size and growth.

b- Indicators of general mortality including crude death rate, life expectancy and total number of deaths.

c- Indicators of infant and child mortality. We will give a brief review of these three indicators. The rising numbers of deaths due to AIDS are expected to result in a reduction of population growth or a decrease in population size. AIDS affects population growth in **two aspects:**
- An increase in deaths.
- A reduction in births.

The mortality caused by AIDS has an impact not only on the population size but also on the age structure of the affected population, the impact of the disease can be shown through age pyramid.

The most immediate effect of the AIDS epidemic is to increase mortality, as HIV-infected adults have a median survival time of 10 years after the infection, the excess number of deaths will occur after attaining maximum prevalence.

DATA

Basic data concerning the spread of the HIV and AIDS epidemic are given in Table 1 and Figure 1. Worldwide, some 245,000 cases of AIDS were reported to the World Health Organization up to April 1990. The registered number of ADIS cases, does not represent the actual situation, it is not the 245,000 cases of AIDS that have been already reported to the (WHO) which will substantially affect mortality, but the estimated 5-10 million HIV-infected persons worldwide. The AIDS-related mortality has to be analyzed in conjunction with all stages of the fatal disease, including the asymptomatic HIV infection. The number of HIV-positive persons aged 15-49 in 2001 was fond to be 1.59 million person in the more developed countries, 1.06 in the Latin America and the Caribbean, while 6.05 million person in Asia . The HIV prevalence among persons aged 15-49 were found to be 1.5%, 18.6% and 7.4% respectively (UNAIDS 2002).

Table 1 AIDS cases, AIDS deaths, and HIV infections by world region (December 1989)[a].

Region	AIDS cases (cumulative)	Estimated no. of AIDS deaths [b] (cumulative)	Estimated no. of HIV infected individuals[c]
Africa	63.842	37.092	Several Millions [d]
Americas	153.720	89.311	Several 100,000
USA	.644	.374	900,000-1,000,000
Europe	33.896	19.694	280,000-800,000 [e]
Oceania	1.976	1.148	Several 10,000
World	254.078	147.619	5-10 Million

[a] Source:WorldHealth Organization (1990).
[b] AIDS deaths have been estimated on the basis of the case fatality rate.
[c] Estimates should be viewed with caution.
[d] Bongaarts and way (1989) have estimated the total number of HIV infected persons in Africa at 2,497,600.
[e] Best estimate according to WHO (1989): 480,000.

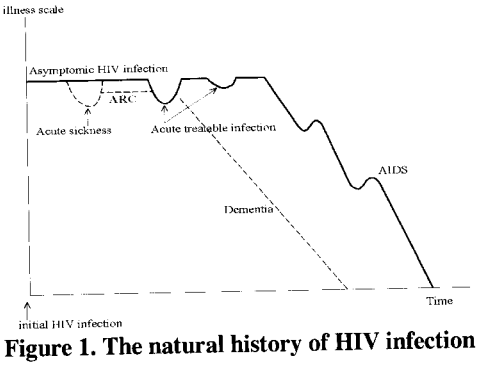

Figure 1. The natural history of HIV infection

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3.1 HIV infection

The prevalence of HIV infection among the population may be only estimated indirectly from limited surveys, the majority has been conducted among high-risk groups (i.e. homosexual, intravenous drug abusers, and prostitutes see Battjes and Pickens 1988).

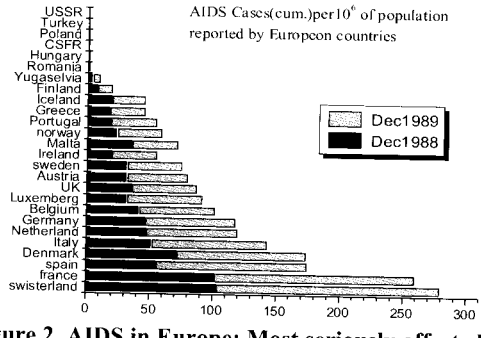


Figure 2. AIDS in Europe: Most seriously affected countries, December 1988 compared with December 1989.

The prevalence rates vary from one country to another and from region to region. The highest rates of HIV infection were found among prostitutes in the urban areas of east and central Africa and the Caribbean (Piot and Careal, 1988).

Several studies (in Nairobi, Mombassa, Kinshasa, and Kampala) have documented infection rates of some 50% to 90%. The increasing prevalence from 1978 to 1985 in three risk groups, homosexual, drug users, and hemophiliacs, in selected cities in the United States and Europe is documented by Melebye et al. (1987). By 1985 prevalence among homosexuals in some selected cities was between 20% in Copenhagen and about 70% in San Francisco and New York; among parenteral drug users, it was between 5% in London and 70% in New York; among hemophiliacs prevalence was from 50% to 70% in London, Hershy, Pennsylvania, and Munich. The trends were still rising in 1985 in all groups, in all selected cities. (See figure3).

3.2 Child bearing women

Several studies have tried to determine the prevalence of HIV among the population by testing pregnant women and their children (Araneta et al., 1988 Archibald et al., 1987; and Armson et al., 1988). An interesting study was conducted by the New York state Department of Health in Albany, New York (Novic et al., 1988). Blood specimens were taken from 25,804 newborn infants in the state of New York, 215 (0.83%) of whom tested positive in HIV. Specimens were taken from 25,804 newborn infants in the state of New York, 215 (0.83%) of whom tested positive in HIV. Seropositivity varied between the regions of New York state; the lowest prevalence rate was found in the Bronx (0.19%); the highest rate among neonates in the Brooklyn (2.29%) and (1.56%). From these figures, we can conclude that rates of HIV infection among women of childbearing age can be found in certain areas of New York City. The number of HIV-positive newborns in 1988 was estimated to be 2240; at least 40% of only 99 women were found to be HIV- positive (0.64%); 54 of the HIV-infected pregnant women were i.v. drug abusers or transfusion patients; 32 had partners with risk factors.

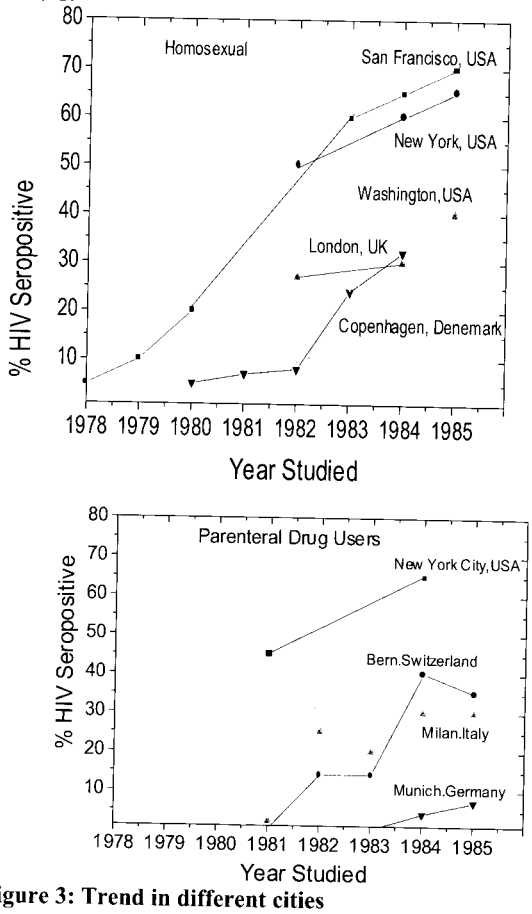
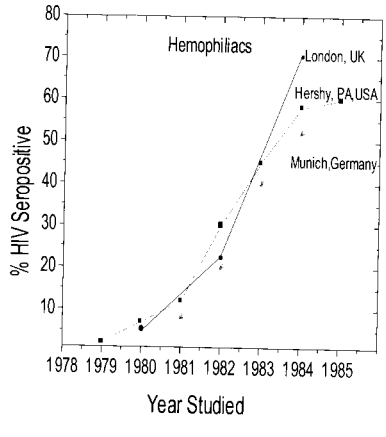


Figure 3: Trend in different cities

Progression to AIDS

Many experts believed that a small fraction of those infected with HIV would develop AIDS. In Germany, for instance the public was informed that between 5% to 16% of those infected ran the risk of developing AIDS, it is obvious that this is a tragic misconception of the natural history of this disease. There is overwhelming evidence that at least 50% of the infected group will develop AIDS in the course of the next 10 years. Since a small fraction (<5%) of HIV –infected persons develop AIDS during the first 12 months after contamination, 20%-25% reach the fatal stage of the diseases within 5 years.



4.1 Survival rate of patients with AIDS

Theoretically there might be a slim chance for an HIV-infected person to avoid the development of AIDS, there is some evidence that all AIDS patients will die within a few years. Up to the present, no therapy is available to eliminate HIV. The average life expectancy of AIDS varies between 1 and 2 years after diagnosis. Lemp and his co-authors (1988a and 1988b) evaluated the survival of 3661 AIDS patients in San Francisco between July 19981 and August 1987. They found a median survival period of only 12.1 months, with a three-year survival rate of 11%, this figure is identical to the results reported by Chang et al, (1988), who conducted a study of 934 AIDS cases, of New York State. Hassig et al. (1988) found that the overall period of survival was even less than one year. In April 1992, 484148 cases were reported, 45% of these cases were in the USA, 13% in Europe, 30% in Africa and 12% in Asia (WHO, 1992a). Figure 4, shows the actual number of persons infected by HIV virus.

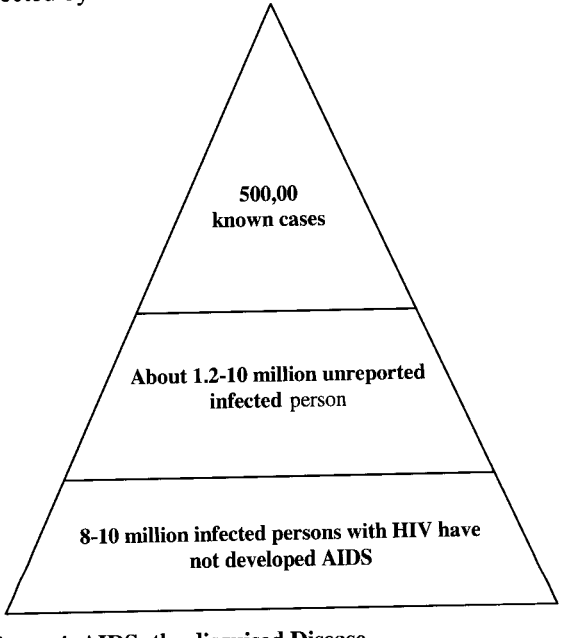


Figure 4, AIDS: the disguised Disease.
Source: WHO 1992a

4.2 AIDS-related mortality

Since the beginning of the AIDS epidemic in the USA, 79587 persons (unpublished CDC data, 1989), also young men, have died of AIDS. Worldwide, the number of AIDS deaths is estimated to be at least 148000. This gives a first hint of the demographic impact of this epidemic. While some information on AIDS related mortality is available from national and international AIDS surveillance systems since the beginning of the epidemic, only few data have been published on AIDS mortality by vital registration system. Recently, the US National Center for Health Statistics (NCHS) has started to report deaths from AIDS among children on the basis of death certificates. According to their statistics, Aids is the ninth leading cause of death of children 1 to 4 and the seventh cause for those 15 to 24 in USA (population today, 1989). If current trends continue, AIDS will be the fifth leading cause of death for those aged 1 to 24 in the near future. Since there is a time lag of two to three years between the HIV epidemic in USA and the spread of the virus in Europe. Galli and his co-authors (1988) evaluated the causes of death among 3127 i.v drug abusers in Italy between 1980 and 1987. McCormick (1988) analyzed mortality statistics in England reference to AIDS from 1984 to 1987; the study demonstrated an increase in the standardized mortality ratio (all causes) for single men aged 25 to 44 between 1985 and 1986.

4.3 Years of potential life lost due to AIDS

Years of potential life lost is defined as the product of deaths in each age interval times the life expectancy at the interval midpoint. The (YPLL) is given in two forms (see Panush and Pertiz 1996), the first allows the familier convention of using the actual life expectancy, the second as the adjusted or illustarative YPLL, substitutes cause eliminated life expectancy at each age in place of the actual life expectancy. An individual whose death is prevented at a given age remains at risk of dying of the cause at a later age, which is what actual life expectancy reflects. The HIV epidemic will have a demographic effect in the future, not only because of the increasing number of AIDS deaths, but even more because of the age structure of the victims. Since AIDS patients die young, they lose many years of potential life (YPLL) (Stevens et al., 1987). We can see from Table 1, AIDS in this three countries was already a frequent cause of death than other infectious or viral diseases, such tuberculosis or viral hepatitis, in 1987. While only 233 of potential life under age 65 were lost due to viral hepatitis in Germany, Aids subtracted 13592 years of potential life from individuals. AIDS caused nearly the same loss potential life before age 65 as diabetes mellitus, 15143 years.

The demographic effects of AIDS in Europe and America are still restricted to a mortality increase in some age groups and in certain regions, this is different in Africa and the Caribbean, in (May 1990) the WHO has estimated that in Uganda infant mortality has increased by 38% due to AIDS. HIV infects one – fourth of the pregnant women in Uganda. According to WHO resources about two million women of productive age are HIV-infected worldwide- most of them in less developed countries. Despite alarming information from Africa and some parts of the third world it is still unclear if AIDS will change the demographic process in these areas.

Projection

It is difficult to project AIDS morbidity and mortality worldwide, since our knowledge of the present state of HIV epidemic is limited (Bailey, 1988). As we have little information on how far the virus spread in less developed countries of Africa and the Caribbean, also it is impossible to tell whether or when there will be a cure and a vaccine that would slow down or stop the epidemic (Brundage et al., 1988).

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In the short run, there can be any doubt that the number of AIDS patients and deaths will increase substantially. For June 1993, Lemp and his co-authors (1988b) have predicted 12349 to 17022 cumulative cases of AIDS in San Francisco. This would be an increase of 107% to 185% over the 5965 cases diagnosed up to August 1988. According to this projection, the number of cumulative deaths from AIDS would be 9966 to 12767 in 1993.

Flandre and Valleron (1988) used a regression analysis to evaluate the expected decrease of life expectancy due to AIDS in France between 1988 and 1990. Compared with the major causes of deaths in 1988, AIDS mortality will have a substantial demographic effect owing to the young age distribution of AIDS patients.

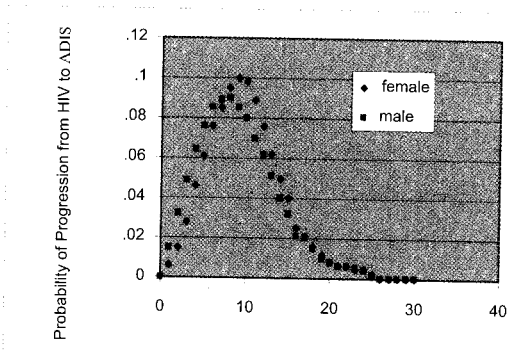

Figure 5 Annual Probability of transition from HIV infection to AIDS.

Modelling the demographic impact of HIV/AIDS

The estimation of the demographic impact of HIV/AIDS may be carried out in three steps; they are as follows:

Step 1: to derive estimates of impact of HIV/AIDS by age and sex, it is first necessary to distribute by sex the yearly number of newly infected individuals.

Although data on the distribution by sex of newly infected individuals are rare, there some evidence suggesting that when HIV/AIDS is spread mainly by heterosexual transmission.

Step 2: Once estimates of newly infected by sex are available, they are distributed by single-year of age according to model age distribution derived from data fitted to Weibull distribution.

Step 3: To estimate the number of deaths due to AIDS by age and sex, the infected population is projected over time using a multi-state approach that takes into account the risks from being HIV-positive to develop AIDS versus the probability of dying of a cause other than AIDS.

The probability schedules used to reflect the chances of developing AIDS after x years of infection (the incubation period) is assumed to follow a Weibull distribution. Different schedules were used for each sex, with a median incubation period of 9.3 years for both sexes combined. The schedules are shown in figure 5.

Conclusion

In short, AIDS epidemic is the result of three successive epidemics. The first happened among homosexual in highly developed countries and among heterosexual urban populations with high-risk behavior in East and central Africa and the Caribbean. Many became contaminated with the virus even before they knew of its existence. The second wave of the epidemic is now under way among I.V. drug abusers in several industrialized countries. Transmission of the virus occurs through contact with infected blood and sexual activity. Heterosexual transmission of the virus is the most rapidly growing

mode of infection in the USA. This heterosexual transmission could trigger a third wave of HIV epidemic in some developed countries. As a result of AIDS prevention campaigns, the spread among heterosexual population in developed countries will be much slower than among homosexuals or drug abusers. While AIDS will remain a serious health problem for several decades, its demographic consequences would be limited.

In Africa, the Caribbean, and some Asian countries the situation seems to be much serious. Since reliable data for these areas are still scarce, it is impossible to accurately forecast the size of the epidemic and its demographic consequences. Since there is as yet no cure for AIDS, and everyone who is infected by HIV dies of the disease, the most immediate effect of the epidemic is to increase mortality. In 2002-2005, the affected countries in Sub-Saharan Africa are expected to experience 14.8 million more deaths than they would have in the absence of AIDS. Among all affected countries, the total number of excess deaths during the period is expected to amount-19.8-million.

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Table: Austria, Switzerland and Germany; Deaths and Years of potential life lost (YPLL) by selected causes of death under age 65 in 1987.

Cause of death	Austria				Switzerland				Germany			
	DEATH	%	YPLL	%	DEATH	%	YPLL	%	DEATH	%	YPLL	%
AIDS	54	.3	1657	.7	95	0.7	2638	1.2	525	0.4	13592	.6
Car Acci[a].	1134	6.0	37626	16.1	727	5.7	23982	10.8	6017	4.0	203533	9
Suicides	1459	7.8	35077	15.0	1155	9.1	28313	12.7	8298	5.5	185845	8.2
Murder	82	.4	2735	1.2	73	0.6	2686	1.2	587	0.4	18338	.8
Diabetes	250	1.3	2385	1.0	153	1.2	1393	0.6	1533	1.0	15143	.7
Liver Cirr[b]	11248	6.6	14740	6.3	402	3.2	4845	2.2	7894	5.3	97990	4.3
Tuberculosis	79	.4	918	0.4	21	0.2	253	0.1	264	0.2	3230	.1
Hepatitis	3	0.0	18	0.0	3	0.0	18	0.0	144	0.1	233	0.0
All causes	18811	100	234242	100	12750	100	222411	100	149682	100	2,254,081	100

Sources: Central Statistics office of Austria, Switzerland and Germany.

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Contribution of Dystocia To Caesarean Section

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الملخص

الهدف: معرفة مدى مساهمة عسر الولادة في العمليات القيصرية وأسباب عسر الولادة. **الطريقة**: تضمنت الدراسة كل حالات الولادة من 1 شهر الصيف إلى 30 شهر الحرث من سنة 2002. **النتائج**: تم إجراء 1206 عملية قيصرية من إجمالي 7974 حالة ولادة من بينها 15% بسبب عمليات سابقة، 18.9% بسبب ضائقة جنينيه، 14.8 % بسبب عسر الولادة. **الاستنتاج**: بينت الدراسة أن العمليات القيصرية الطارئة هي أكثر حالات العمليات القيصرية حدوثاً وأن عسر الولادة هو السبب الرئيسي لها.

Abstract

Background: The increase in the rate of cesarean section in our hospital over the last 10 years has always been of concern. **Objective:** To find the true contribution of dystocia to overall cesarean section and the causes of dystocia. **Setting:** Al – Jamahiria hospital, department of Obstetrics and Gynecology, Benghazi, Libya. **Materials and Methods:** The study included all patients who were admitted to the labour ward between June 1st and November 30th after diagnosis of labour, the patient was monitored for progress of labour. Failure of progress is diagnosed when cervical dilatation at a rate of less than 1cm per hour or when there is secondary arrest in the first stage or the second stage of labour that initially progressed normally. **Results:** We had 7974 deliveries,1759 primigravida, 6215 multigravida.1206 caesarean sections (15.12%) repeated caesarean section ((32.84%), fetal distress (18.90%), dystocia (14.80%), breech (8.21%), others (25.24%). We had 215 cases of previous caesarean section in labour. 89 cases induced by prostaglandin. We had 178 cases of dystocia (14.8%), 50 primi and 128 were multi. We had 53 cases (24.65%) had repeated caesarean section because of dystocia, the causes of dystocia failed induction (6.18%), CPD (29.77%), O.P. (26.96%), inefficient uterine action (16.85%), malpresentation (20.22%), 17 cases taken for previous caesarean section at fully dilated cervix. **Conclusion:** The study showed that emergency cesarean section is the largest category of caesarean section (38%) of overall cesarean sections and dystocia is the single, most common primary indication for cesarean section (14.8%) which comprised (39.2%) of emergency caesarean section. Also we managed labour suboptimally before making the diagnosis of dystocia.

Key words: Dystocia, Caesarean section, Labour.

Introduction

Dystocia is defined as abnormal progression of labour. Dystocia is the indication for one half of primary caesarean section.

It could be the result of:

i) abnormalities of the expulsive forces

ii) abnormalities of presentation.

iii) abnormalities of maternal pelvis or birth canal.

Dystocia is diagnosed when there is failed induction- no cervical dilatation after repeated priming with prostaglandins or failure of the cervix to dilate beyond 3cm after at least 6 hours of adequate oxytocin treatment. Persistent occipitoposterior. Cephalopelvic disproportion - failure of the head to descend at fully dilated cervix in the presence of adequate uterine action. Dysfunctional labour – a rate of cervical dilatation of less than 1cm/hr during active phase of labour. Dystocia is associated with increased maternal and fetal mortality and morbidity. Treatment of dystocia which includes caesarean section is also associated with increased maternal morbidity and mortality. Moreover, it has been documented that the steep rise in caesarean section rate over the last 20 years has not been responsible for the dramatic improvement in prenatal mortality observed during that time[1,2]. Therefore, careful diagnosis and proper management of normal labour and early diagnosis and treatment of failure of progress will decrease the rate of primary caesarean section and the overall caesarean section [3,4,5,6,7,8,9].

Aims of the study

I. To find out the true contribution of dystocia to the overall caesarean sections in our hospital.

II. To find out the causes of dystocia.

Materials and Methods

A prospective study was carried out between June 1st and November 30th, 2002 at Jamahiriya hospital, Benghazi, Libya. The study included all patients who were admitted to the labour ward. A detailed medical and obstetric history was taken. General, abdominal and vaginal examinations were done. During labour, the patient is monitored for progress of labour. Failure of progress is diagnosed when cervical dilatation at a rate of less than 1cm per hour in the presence of efficient uterine contraction or when there is secondary arrest in the first stage or the second stage of labour that initially progressed normally. It is considered that an efficient contractions is a contraction which lasts for more than 40

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seconds and three or more contractions in 10 minutes. Condition of the fetus was examined by:

i) observation of liquor for meconium staining.
ii) by intermittent auscultation of fetal heart rate every 15 minutes in first stage and after each contraction in second stage. Patients with uncomplicated previous one caesarean section were allowed for trial of vaginal delivery. Also vaginal delivery of breech was allowed when estimated weight was <3.8 kg with well flexed head by ultrasound scanning.

Results

There were 7974 deliveries between June 1st and November 30th in the year 2002, of whom 1759 were primigravida, 6215 were multigravida.1206 caesarean sections which were performed either as elective for first caesarean section, elective repeated caesarean section, emergency before labour caesarean section, emergency during labour caesarean section. The indications for caesarean section are shown in Table I.

Table I: Indications for caesarean section

Indications for caesarean section	Number of cases	
Repeated caesarean section	396	(32.84 %)
Fetal distress	228	(18.90 %)
Dystocia	178	(14.80 %)
Breech	99	(8.21 %)
Others	305	(25.24 %)

215 cases of previous one caesarean section in labour. 89 cases induced by prostaglandin.

178 cases (14.8%) of caesarean section because of dystocia, 50 were primigravida and 128 were multigravida, 53 cases (24.65%) which had repeated caesarean section because of dystocia, 11 of them had previous caesarean section also because of dystocia. We subdivided the dystocia cases into 5 subgroups as shown in Table II.

Table II: Dystocia groups.

Causes of dystocia	Number of cases	
Failed induction	11 cases	(6.18 %)
Cephalopelvic Disproportion	53 cases	(29.77 %)
Occipitoposterior	48 cases	(26.96 %)
Inefficient uterine action	30 cases	(16.85 %)
Malpresentation	36 cases	(20.22 %)

11 cases of failed induction: 4 induced by prostaglandin, 7 induced by artificial rupture of membrane, 30 cases of inefficient uterine action: 21 were primi, 9 were multigravida.

27 cases taken for caesarean section at fully dilated cervix: 17 cases with no time given in the second stage, limited time given in 10 cases of which vacuum delivery was tried in 6 cases.

The mean duration of labour was 9 hours. The mean birth weight for babies of dystocia cases was (3.45kgm).

Discussion

The increase in the rate of caesarean sections over the last 10 years in our hospital has always been our concern. This study aims to find out the true contribution of dystocia to overall caesarean sections.

We compared our results with the work done by Lena M. Macara et al. during 1991 at Queen mother's hospital Glasgow, the United Kingdom. Our caesarean sections rate was (15.12%) which is close to their rate (16.3%). Emergency caesarean sections in labour was the largest category of caesarean sections in our hospital (38%) of the overall caesarean sections compared to their rate (42%). Dystocia was the single most common primary indication for caesarean sections (14.8%) which comprised (39.2%) of emergency caesarean sections. This compares favorably with their results; dystocia rate was (16%), comprising (40%) of their emergency caesarean sections. From these results, if efforts addressed to prevent and treat dystocia, approximately half of primary caesarean sections could be avoided and then many subsequent repeated caesarean sections will be unnecessary. The mean duration of labour of dystocia cases was 9 hours and 10.7 hours in their cases, which means that longer time was given for their cases. The mean birth weight for babies of dystocia cases was (3.45kg) which is equal to their result (3.5kg). That means macrosomia is not a problem in our dystocia cases. The majority of dystocia cases were spontaneous laborers (93.81%) while (6.18%) were induced compared to their (78%) were in spontaneous laborers while (20%) were induced, this difference is explained by the higher hospital induction rate they have (21%). We subdivided dystocia cases into 5 subgroups as shown in Table II. The overlap among the groups was present but caesarean section was ascribed to only one of those 5 groups. They subdivided dystocia cases into 4 groups: O.P. (47%), dysfunctional labour (26%), CPD (14%), failed induction (13%). Comparing the two studies, we may see that we have a higher rate of CPD cases (29.77%) while they had (14%). So we may have overdiagnosed CPD. Also they used oxytocin in all dystocia cases while we used it in only (26.4%) of the cases. That means we managed labour suboptimally before making the diagnosis of CPD. We had (6.18%) of dystocia cases because of failed induction compared to their (13%). Their higher rate is due to the higher hospital induction rate (21%); and as we know dystocia is higher with induction than with spontaneous labour [9]. They had higher O.P. cases (47%) compared to our (26.96%) and this is due to their higher number of primigravida cases. Their primigravida percentage was (45.63%), Compared to our (22.6%) and as we know O.P. is

more in primigravida[10]. Also they had higher dysfunction labour (26%) compared to our (16.85%), this is because half of their deliveries were primigravida and inefficient uterine action is common in primigravida but rare in multigravida[11]. From our study we notice that active management of labour was not applied. Oxytocin was used in only (26.4%) of dystocia cases. Even though they used oxytocin in all of their cases (100%), usually undertaken late, we have reached the same conclusion they obtained which is that active management of labour can correct dysfunction labour and malrotation of fetal vertex and does reduce c/s rate for dystocia, and this was proved by work done by O'Driscoll and Meagher at the National Maternity Hospital, Dublin[12,13,14,15,] and was also demonstrated in randomized and controlled trials in the USA.

Conclusion

Even though other causes of caesarean sections are important contributors to the overall rate of caesarean sections in our hospital, improved management and treatment of dystocia may reduce the primary caesarean section and the overall caesarean section rate. Active management of labour seems to be the most useful approach to reduce the caesarean section rate attributed to dystocia.

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Diabetic Ketoacidosis in Benghazi Characteristics and Outcome in 211 Patients

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الملخص

مقدمة: الحماض الكيتونى السكري سبب متكرر من أسباب المراضة والوفاة لدى مرضى السكرى، المعلومات عن أسباب الحماض الكيتونى ونسبة الوفيات غير معروفة بنسبة كبيرة وخاصة في ليبيا . **الهدف**: توضيح أهمية التعليم الصحى السكرى فى منع الحماض الكيتونى **المكان**: أجريت هذه الدراسة في بنغازي عن 211 مريضاً بالحماض الكيتونى فى الفترة من يناير 1997- ديسمبر 1999 . **النتائج**: وجدنا أن 59.2 % من المرضى كانوا من الإناث وأن الحماض الكيتونى كان هو المؤشر الأول للسكر عند 29.9 % . فقرا لمطاوعة كان السبب الأكثر شيوعاً بين المرضى 63.5 % . المرضى القدامى كان معدل السكر لديهم أعلى ونسبة الأس الهيدروجيني (الباء هاء) أقل من المرضى الجدد الذين أمضوا فترة أطول في المستشفى و كانت نسبة الوفيات 3.8 % .

Abstract

Background & objectives: Data on precipitating factors, morbidity and mortality due to Diabetic ketoacidosis (DKA) from Libya is scarce. **Setting & methods:** In this paper we report precipitating factors, presentation, management and mortality of 211 consecutive DKA patients admitted to 7th October teaching hospital during Jan.1997- Dec.1999. **Results:** There were 125 (59.2%) females and 86 (40.8%) males and in 63 (29.9%) patients DKA was the initial manifestation of diabetes. Poor compliance was the main precipitating factor in 94 (63.5%) of known patients .The majority of patients (74.4%) were conscious. Known patients had higher blood glucose (30.7 ± 6.4 mmol/L *vs* 28.3 ± 7.4 mmol/L) and shorter hospital stay (6 days *vs* 10 days) than newly diagnosed . There were 8 deaths (3.8%). **Conclusion:** This data highlights the importance of diabetic health education as a preventive measure of DKA.

Introduction

Diabetic Ketoacidosis (DKA) is one of the serious acute complications of diabetes and it is potentially fatal. Faich et al found an annual rate of 46 per 10000 diabetics, and in the majority (85%) it was preventable[1]. It has been suggested that the incidence of diabetic ketoacidosis might serve as an index of the quality of medical care[2]. Data on precipitating factors, presentation and outcome from Libya are scarce. The objectives of this prospective study were to describe the clinical features presentation precipitating factors and mortality among Libyan diabetics in Benghazi.

Materials and Methods

All consecutive patients aged 15yrs and above and admitted with DKA to medical wards of 7th October teaching hospital in Benghazi, during 3 year period Jan. 1997- Dec. 1999.

Criteria for inclusion in the study were: First blood glucose ≥ 16.6 mmol/L, first blood PH < 7.3, first bicarbonate < 15 mmol/l, together with marked ketonurea.

Investigations included blood glucose (by Glucose Oxidase method using Beckman glucose analyser), arterial PH (by gas specific electrodes in AVL blood gases analyser), serial serum electrolytes (using electrode specific Na, K analyzer), and blood urea (by Beckman blood urea analyzer using the buffered urease to convert ionic urea to ionic ammoniumbiacarbonate).

Other investigations were performed on the basis of the clinical condition of the patient

Data included: age, sex, duration of diabetes, type of treatment, previous episodes of DKA, presenting symptoms, precipitating factor and level of consciousness: fully conscious if oriented, obeying and speaking spontaneously. Drowsy if confused or inappropriate talking. Comatosed if not responds to speech or painful stimuli. All patients were treated with intravenous fluids, and potassium supplementation as suggested by Keen and Jarret [3] together with low dose insulin either hourly intramuscularly or as a continuous intravenous infusion.

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Table I: Patients Characteristics

Character	Known Diabetics		Newly Diagnosed		Total
	Male	Female	Male	Female	
No. patients	53	95	33	30	211
Type of Diabetes Type 1 Type 2	 40 12	 76 20	 - -	 - -	 116 32
Type of treatment Insulin Oral drugs	 51 2	 89 6	 -	 -	 140 8
Mean age ± sd	29.4 ± 13.2	27.3 ± 11.5	27.9 ± 9.4	29.9 ± 10.3	
Mean duration of Diabetes ± sd	9.1 ± 6.5y	8.7 ± 5.36 y	-	-	
Conscious Level: **Conscious** **Drowsy** ***Comatosed***	 39 11 3	 74 19 2	 23 9 1	 21 8 1	157 (74.4%) 047 (22.3%) 007(03.3%)
Mortality	4	2	1	1	8 (3.8%)

Table II: Precipitating factors

Precipitating factors	Males (%)	Females (%)	Total
Poor Compliance Omission of Treatment Dose Frequency Reduction Social Problem	30 (56.6) 18 12 -	64 (67.4) 46 14 4	94 (63.5) 64 26 4
Infections Urinary Tract Upper Respiratory Tract Lower Respiratory Tract Pulmonary TB Acute Cholecystitis	16 (30.2) 4 5 6 1 -	28(29.5) 15 7 4 0 2	44 (29.7) 19 12 10 1 2
Myocardial infarction Stroke Others	2(3.8) 2 (3.8) 3 (5.7)	1 (1.1) - 2 (2.1)	3 (2) 2 (1.4) 5 (3.4)
Total	53(100)	95 (100)	148 (100)

Table III: Laboratory data at presentation

Lab. Parameter	Known Diabetics	New Diabetics	*P.*Value
Blood Glucose	30.7 ± 6.4 mmol/L	28.3 ± 7.4 mmol/L	$P < 0.05$
Serum Sodium	133 ± 5.3 mmol/L	138.4 ± 5.8 mmol/L	$P < 0.05$
Serum Potassium	4.7 ± 0.1 mmol/L	4.4 ± 0.5 mmol/L	$P < 0.05$
Arterial PH	7.05 ± 0.12	7.12 ± 0.13	$P < 0.05$
Bicarbonate	8.9 ± 3.2	10.4 ± 3	$P < 0.05$
Blood Urea	14.1 ± 6.4 mmol/L	10.7 ± 6.6 mmol/L	$P < 0.05$

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Results

There were 211 patients (125 females, 86 males) M: F ratio 1: 1.5 and 148 were known diabetics and 63 (29.9 %) were newly diagnosed. The mean age of known diabetics was 28.9 ± 13.2 yrs (15-83) yrs and mean age of newly diagnosed patients 29.6 ± 13.2 yrs (17– 58) yrs. Duration of diabetes was 8.8 ± 5.8 yrs (1-28) yrs. Eighteen patients of newly diagnosed (28.6%) were above 40 years.

Among known diabetics 95 were females (64.2%) and 53 were males (34.8%). One hundred-sixteen (78.4%) were known cases

of type 1 diabetes and 32 (21.6%) were known cases of type 2. Twenty four patients (75%) of type 2 were on insulin because of drug failure or complications, and 8 (25%) were on oral hypoglylemic agents.

Among known diabetics, 121 patients had one episode of DKA during study period and 10 (8.3%) had 27 episodes. All patients with multiple DKA episodes were type 1 females.

Precipitating factors (Table II), poor compliance was the precipitating factor in 94 cases (63.5%). In 64 cases (68.1%), the patients omitted insulin injections because of pain and inconvenience. In 26 cases (27.7%) the patients reduced the frequency of injections, and in 4 cases (4.2%) of females, the patients stopped treatment because of family problems and they were among the patients with multiple DKA episodes. Infections were the other major cause in 44 cases (29.7%). (Table II)

Presenting Symptoms.

Polyurea and polydipsia were present in 112 patients (53%) and infections in 44 (20.9%). At presentation the majority 157 Patients (74.4%) were conscious GCS 15/15 and only 7 (3.3%) were comatosed GCS < 8/15. see (Table I)

Initial laboratory findings: (Table III)

Initial blood glucose was higher among known patients 30.7 ± 6.4 mmol /L than newly diagnosed patients 28.3 ± 7.4 mmol /L ($P<0.05$). Serum potassium and blood urea were higher among known patients than newly diagnosed. Known patients had lower serum sodium, lower arterial PH and bicarbonate than newly diagnosed patients.

Length of stay: Known patients had mean length of stay of 6 days (4-13), and 10 days (7-24) among newly diagnosed patients.

Mortality: There were 8 deaths (3.8%), six deaths occurred in known patients and two newly diagnosed. Deaths were due to acute MI (2), CVA (1), septic shock (3) and in (2) undetermined cause.

Discussion

Before the introduction of insulin DKA was universally fatal. Our study showed that 21.6% of known patients were type 2 and this was lower than 44.7% in Saudi Arabia[4], 55.2% in South Africa [5]and 62.8% in India[6]. An important finding in this report was that 29.9% of patients had DKA as initial manifestation of the diabetes; this figure is higher than 10% in Saudi Arabia[4], 19% in Saudi Arabia[7] and 22.7% in Taiwan [8]. These high levels of 29.9 % of newly diagnosed in addition to the finding that 33.3% of them were 40 years and above are alarming. Of the 10 patients with multiple DKA, 4 had family problems, highlighting the importance of social workers as part of the diabetes team. Poor compliance was the leading cause of DKA in this study (63.5%) this was comparable to reports from Saudi Arabia [4,7] and Libya [9]. Lack of money to purchase insulin was responsible for DKA in some socities [10], in our patients omission of treatment was due to lack of diabetes health education rather than lack of anti-diabetic treatment which is free of charge. The low coma rate 3.3% compared to 11% in Pakistan[11] may be due to easy access to medical facilities which are free of charge.

Newly diagnosed patients had longer hospital stay because of the need to control their blood glucose level and to train them how to take injections. A mortality rate of 3.8% was significantly lower than other reports of 6.8% in South Africa[5], 6.3% in India [6], 8% in Pakistan [11] and 32% in Nigeria [12] but comparable to 4.1% and 3.5% in Saudi Arabia[4, 7] and 5.1% in Libya [9]. The high mortality rates in many developing countries has been related to delay in diagnosis and treatment which is further aggrivated by the absence of emergency laboratory services and drug shortage in their hospitals[12]. The low mortality rat in our study is probably due to easy access to medical services and availability of equipped laboratories and facilities for intensive care. We conclude that DKA occurs among both type I and type 2 Libyan diabetics but with low mortality and in the majority it is preventable.

The results also high lights the importance of diabetes health education for both patients and their care providers.

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Childhood Immunethrombocytopenic Purpura Amina M. Beayou; Nureddin A. Daghman

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الملخص

أكثر الأسباب شيوعاً والتي تؤدى إلى نزف الدم هي فرفرية قلة الصفيحات المجهولة السبب ومن النادر أن يهدد حياة الطفل والسؤال الذي يطرح في هذه الدراسة هو متى يجب البدء في العلاج. **الهدف** من هذه الدراسة هو مراجعة التطبيقات العلمية وتحديد المسارات العالمية للتشخيص والعلاج بمستشفى الفاتح للأطفال – بنغازي. **الطريقة** 70 حالة اقل من 15 سنة تمت دراستهم بشأن بعض المقاييس التي تشمل أعراض المرض الابتدائية وعدد الصفائح الدموية والعلاج. **النتائج** نسبة الحدوث السنوي في بنغازي 2.8 % لكل 100.000 طفل. الأعراض الابتدائية كانت حدوث نزف في الأغشية المخاطية 53 % والجلد 37 % . عدد الصفائح الدموية الأولى كان أقل من $20x10^9$ لكل لتر في 59% من المرضى. تم فحص نخاع العظم في 99% من المرضى، العلاج الابتدائي أعطى لي 63% من الحالات. 55% تمت معالجتهم بالكورتيزون. تم نقل الدم أو الصفائح الدموية لي 13% من المرضى. **الاستنتاج**: هناك ميول لمعالجة المرض طبقا لعدد الصفائح الدموية بغض النظر عن الأعراض حيث استخدمنا في دراستنا نقل نواتج الدم وتكرار فحص نخاع العظم متبعين في ذلك الخطوط العالمية لتشخيص وعلاج حالات فرفرية قلة الصفيحات المجهولة السبب.

Abstract

Background: Immune thrombocytopenic purpura (ITP) is the most common bleeding disorder in children. Though life threatening haemorrhage is rare, the question of when to treat it is still widely debated. **Objective**: To review local practice and determine the necessity to establish national guidelines in respect to diagnosis and management. **Setting**: Al-Fateh Children Hospital in Benghazi. **Patients and Methods**: Seventy cases, less than 15 years of age, were retrospectively studied and analysed regarding various parameters including initial manifestations, platelet counts and treatment. **Results**: The annual incidence of ITP, in Benghazi, is 2.8/100,000 children. Mucocutaneous and cutaneous bleeding were the initial manifestations in 53 % and 37 % of patients respectively. Initial platelet counts were less than 20 x 10^9/L in 59 %. Bone marrow examination was performed in 99% of the cases. Initial treatment was given to 63 % of cases, of these 55 % received steroids. Whole blood and/or platelet concentrates were given to 13 % of patients. **Conclusion**: There is a tendency to treat patients according to platelet counts rather than symptoms with more frequent use of blood products in our study, together with the high frequency of bone marrow examination mandates the urgent need to set national guidelines in respect to diagnosis and treatment of ITP.

Key words: Children, immune, purpura, thrombocytopenia.

Introduction

Immune thrombocytopenic purpura (ITP) is the most frequent cause of haemorrhagic diathesis in children less than 15 years of age. Despite the spectacular appearance of the affected child with bruises and ecchymotic patches covering almost all the body. Life-threatening bleeding like cerebral haemorrhage is exceedingly rare[1,3]. In the majority of cases ITP is a self limited disorder[4,6]. However, the arising situation of very low platelet counts in the face of mild disease provoked a continuing debate regarding treatment[7,9]. Studies from different countries were conducted to elaborate on the clinical manifestations at presentations and management of ITP[10, 12]. We conducted this retrospective study, involving those children admitted to El-Fateh Children Hospital in Benghazi during the period from January 1995 to December 1999, to shade light on our experience with childhood ITP with particular attention to diagnosis and management.

Materials and Methods

This study was conducted at El-Fateh Children Hospital in Benghazi which is a referral centre for the eastern part of Libya. The medical file of every child, less than 15 years old, diagnosed with ITP and admitted to this hospital during a period of 5 years was analyzed.

The data selected included age, sex, clinical features at presentation, follow up platelet counts, bone marrow assessment, initial treatment, and outcome. It is a customary practice in this hospital to admit such cases to the general medical ward. Therefore the proper diagnosis of ITP was left to general paediatricians in their respective units. The diagnosis is based on excluding other causes of thrombocytopenia. Bone marrow samples were reviewed in the majority of cases by the second author.

Results

In a period of 5 years a total of 70 cases (36 females, 34 males) with ITP, aged 5 months to 13 years, were admitted to this hospital. Of these, 45 cases were from Benghazi city and the remaining 25 cases were from other parts of eastern Libya. This implies that each year about 9 new cases of ITP, from Benghazi city, are admitted to the hospital. Accordingly the annual incidence of ITP, in Benghazi city, was esti-

mated to be 2.8 per 100,000 children less than 15 years of age.

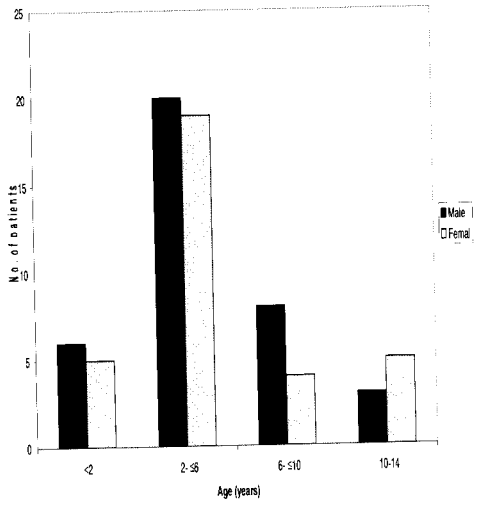

Figure 1: age and sex distribution of patients.

Figure 1 shows male predominance in the age group below 10 years; however in the overall data there is slight female predominance (1.06:1). The age group most frequently affected is 2 to 6 years of age. Regarding clinical presentation, 26 patients (37%) presented with isolated cutaneous haemorrhage only and 6 patients (9%) had mucosal bleeding only. Mucocutaneous bleeding was seen in 37 patients (53%). 13 Patients (19%) had melena and/or haematuria. One child had no bleeding symptoms at diagnosis. He was discovered by chance during routine blood examination for unrelated illness his platelet count was $66x10^9$/L. For all patients the initial platelet count at presentation ranged from 2 to $102x10^9$/L. Forty one patients (59%) had platelet count < 20 $x10^9$/L and 16 patients (23%) had count <10x 10^9/L. It is worth mentioning that patients with platelet counts more than $80x10^9$/L had had initial counts less than that before referral to this hospital. However, for the purpose of this study we decided to quote initial counts on admission to this hospital.

Bone marrow examination was performed in 69 cases (99%). In most of the cases megakaryocyte counts were increased or normal.

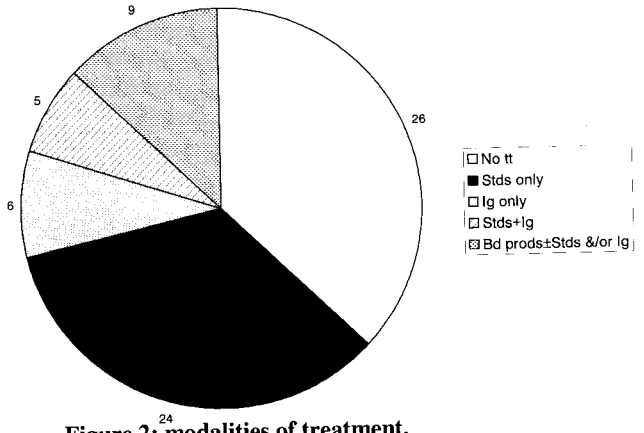

Figure 2: modalities of treatment.
tt=treatment;stds=steroids;ig=immunoglobulin; bd prods= blood products.

Regarding treatment, 26 patients (37%) received no treatment. The remaining 44 patients (63%) received various modalities of medical treatment of those 24 patients (55%) received prednisolone in a dose of 2 mg/kg/day. Whole blood and/or platelet concentrates were given to 9 patients (13%) 7 of them were transfused outside Benghazi in their respective hospitals. Four patients received whole blood. In one patient the pre-transfusion haemoglobin (Hb) level was 116g/L, in the other 3 patients no pre-transfusion Hb levels were available but their post-transfusion Hb levels were ≥140g/L. Two patients each with initial platelet count of $9x10^9$/L received platelet concentrates. Three patients received both whole blood and platelet concentrates. In two patients the pre-transfusion Hb levels and platelet counts respectively were 110g/L and $8x10^9$/L, and in one patient the post-transfusion counts were 150 g/L for Hb and $13x10^9$/L for platelet. Platelets concentrates were given in this hospital. No life threatening bleeding was documented and no post-transfusion increments were calculated in any of the cases. Figure 3 shows number of patients in relation to platelet count and treatment.

On discharge from the hospital platelet counts were available for 60 patients only: 47 (78%) had counts $>50x0^9$/L, while 13 (22%) had counts $<50x10^9$/L of those followed up 5 patients (7%) had persistent low platelet counts for more than 6 to 12 months. However, none had major bleeding problems. Splenectomy was performed for one patient. One case had LE cells in peripheral blood examination, but no other supportive evidence for autoimmune disease was found.

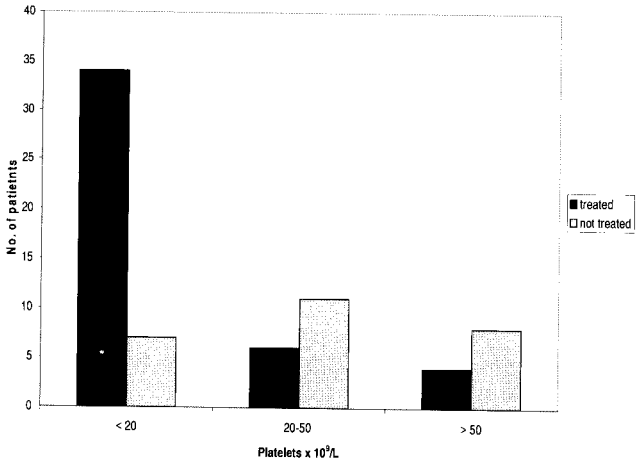

Figure 3: number of patients in relation to platelets count and treatment.

Discussion

Our efforts to obtain a precise figure for the incidence of ITP are hampered by the lack of national registry and by the fact that not all cases of ITP from the eastern province are referred to this hospital. However, it is a customary practice, in the Benghazi area, to refer any child with bleeding tendency to this hospital for further assessment and these patients are usually looked after inside the hospital. Nevertheless some patients whose platelet counts are not low enough to cause symptoms may escape medical attention. In this study, for example, one of the patients was discovered by chance as forementioned. Such difficulties jeopardise also attempts by other study groups to precisely determine the incidence of ITP in children[2,4,10,13]. Our results indicate that the incidence of ITP, in Benghazi city, is about 2.8 per 100,000 in children less than 15 years of age. This figure is close to that of Denemark[10] (2.9/100,000) and U.K.[6] (3/100,000). The incidence in Norway[11] is much higher (5.3/100,000). The Sheffield[2] group reported a high incidence (4.8/100,000) as well. The disparity in reported incidence by various groups may be arbitrary rather than a genuine one. Lack of accurate registry and loss of patients, as in large studies, may account for the low incidence in some studies. ITP may occur at any age albeit it is most common in children less than 10 years of age. As reported else where we found that children aged 2 to 6 years, a period associated with frequent exposure to viral infections, are the most commonly affected [14, 15, 16].

The majority of our patients presented with mucucutaneous manifestations ranging from purpuric rash with epistaxis and/or gum bleeding to association with melena and/or haematuria in about 19 % of them. Though it has been widely quoted that the incidence of intracranial haemorrhage (ICH) is 1-3 %, more recent studies[2] demonstrated that it is actually closer to 0.1-0.5%. In an international registry out of 2031 children with ITP only two patients had ICH[1]. In the current study none of our patients presented with or developed, during the course of the disease, life threatening bleeding like ICH.

Many studies have demonstrated that in the typical case bone marrow examination is not indicated[17,19] unless steroids are to be started[20]. In fact the international guidelines consider it mandatory in this perspective[16,21]. Failure to do so may lead to overlooking a diagnosis of leukaemia with the devastating consequence of seeing the patient in his first relapse[22]. In our study about 99 % of patients had bone marrow examination done. This is a rather very high figure particularly in view of the fact that 37 % of patients had received no treatment. This may reflect the medical attitude, probably among the junior medical staff, that steroids will soon be started and therefore a bone marrow aspirate should be performed before hand.

The clinical situation of very low platelets in the face of mild disease provoked a continuous debate, probably since the time of Werlhof who first described this disease in the 18th century[23], regarding whether to treat ITP or not. National treatment guidelines were developed in different countries to refine the therapeutic approach [16,24] but even this failed to achieve a consistent practice in any one country[4]. In our study about 63% of patients have received some form of initial treatment. This correlates to a large degree with the percentage of those presented with platelet counts less than 20 x 10^9/L (59%), indicating that the decision for initiating treatment is rather driven by platelet counts. It seems this is an inherent problem in the management of ITP everywhere. In three studies conducted separately in England[4], Norway[11] and Germany[25], it was shown that 60%, 68%, and about 80%, respectively, of the patients were medically treated. In all these studies treatment was driven by the platelet count at presentation. There is always a fear that patients with very low platelet counts may develop a fatal ICH but the fact that treatment does not prevent such complication[26] makes the decision of no treatment a reasonable one as well. Blood products, other than immunoglobulins, were given to 13% of our patients. Seven (28%) of the 25 patients, from outside Benghazi, received whole blood with no obvious indications. Furthermore, 5 transfusion episodes of platelet concentrates were given in our hospital again with no clear indications. The administration of blood

products is not without hazards and therefore they are not expected to be prescribed lightly. This further highlights the fact that ITP in children remains an elusive condition that can be difficult for the general paediatrician to treat[27]. The urgent need for national guidelines in respect to diagnosis and management of childhood ITP cannot be over emphasized.

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Analysis of Frequency, Types and Distribution of Jaw Cysts in the North Eastern Region of Libya

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الملخص

أهداف الدراسة: معرفة صفات أكياس عظام الفكين فى شمال شرق ليبيا. **طريقة البحث:** دراسة تحليلية لأكياس وُجدت بعظام الفكين لدى ٤٢٢ مريضاً تراوحت أعمارهم ما بين ٩ و ٧٢ سنة. شُخصت تلك الأكياس سريريا و إشعاعيا ومن ثَم خضعت للفحص المجهري. أخذت العينات في الفترة من شهر ١ سنة ١٩٨٩ حتى شهر ٦ سنة ٢٠٠٣ (شكلت ١٦,٥% من مجموع العينات التي تم إجراؤها في الفترة تحت هذه الدراسة). **النتائج و الإستنتاج:** أظهر تحليل المعلومات المستقاة من دراسة البيانات المتعلقة بعمر وجنس المرضى والمكان التشريحي للأكياس بأن عدد الذكور يربو على عدد الإناث بنسبة ١:١,٧ وأن الأكياس الالتهابية هي النوع الأكثر شيوعا. أتضح أن نمط توزيع الأكياس استنادا إلى عمر المريض مشابها للدراسات السابقة، حيث أن ٦٦% من الأكياس ظهرت عند أشخاص تقل أعمارهم عن ٣٠ سنة. كما لوحظت كذلك اختلافات بينية في التوزيع التشريحي لمكان ظهور الأكياس بما أن ٦١,٨% منها ظهر في الفك العلوي بينما ظهر ٣٨,٢% فقط منها في الفك السفلي. كانت معظم أكياس قمة الجذر في منطقة القواطع الجانبية العليا، و الأكياس المسننة في منطقة نواجذ العقل السفلية، أما الأكياس السنية الكيراتينية ففي المنطقة بين الطواحين السفلية و الفرع الراد للفك السفلي، أما الأكياس المتبقية بعد الخلع الجراحي للسن فكان معظمها في الفك العلوي

Abstract

Objectives: To determine the characteristics of jaw cystic lesions in North Eastern Libya. **Patients & Methods**: Analytical study of intrabony cystic lesions of the jaws in 4٢٢ patients (9 to 72 years old). The cysts had been diagnosed clinically and radiographically and subjected to histopathological examination. Biopsies had been performed from January 1989 through June 2003 (those accounted for 16.5% of the total biopsied lesions during the period under review). Data were analyzed with regard to age, sex and anatomical distribution. **Results & Conclusions:** males outnumbered females at a ratio of ١,٧ to 1, and inflammatory cysts were the most common. The pattern of cyst distribution according to age groups was similar to those found in previous studies, as about 66% of cysts occurred in persons below 30. Anatomical site variations were noticed since as much as 61.٨% of cysts occurred in maxilla and only 38.٢% of them in mandible. Most radicular cysts occurred in the maxillary lateral incisors area, dentigerous cysts in the mandibular wisdom teeth area, while odontogenic keratocysts in the region between the mandibular molar teeth and ramus of the mandible and most postoperative residual cysts appeared in maxilla.

Keywords: Odontogenic Cysts, Libyan Population, Jaw Bone, Oral Health.

Introduction

Cysts are among the most prevalent pathological conditions occurring in the maxillofacial region[1,3], most of them are intrabony and their lining epithelium is derived from developing dental apparatus, although there is still some small percentage of pseudocysts and extraosseous appearances[4]. Thus the type of odontogenic cysts is dependent chiefly upon the stage of odontogenesis during which they originate [5].

The system of classification of cysts and tumors in the maxillofacial region and their nomenclature is still under continuous adjustments and amendments. These alterations (to some extent) are due to the diversity of such lesions and taking the advantages of the vast advances in biological sciences (especially molecular biology and immunology) that resulted in better understanding of the origin, pathogenesis and clinical course of these lesions[5]. Although initial clinical diagnosis of jaw cyst can be made on clinical grounds and radiographic features, the final diagnosis, however, can only be achieved through histopathological examination[6,7]. The later is also helpful in excluding the otherwise more aggressive lesions with similar appearance [8].

This study was carried out in the dental faculty of Benghazi that (throughout the period of this study) was the only specialized center conducting diagnosis and carrying out the management of orofacial disorders in the entire north eastern region of the country, serving an estimated 1.25 million people [9].

An early diagnosis and swift management of cystic lesion of the jaw is of great importance in dentistry, as most of these cysts (especially the odontogenic variety) continue to grow and expand and rarely regress [10]. Thus a cyst may perforate cortical plates of jaw bone rendering it susceptible to pathological fracture, or it may involve bigger areas with huge devastation and devitalization and loosening of nearby teeth[11], or in few occasions it may get secondarily infected[12] and thus may act as a focus of infection [13]. Malignant transformation activity is known to occur in the lining wall of few of them especially the dentigerous cyst[14,15].

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This retrospective study details the findings about the frequency of different types of jaw cysts in regard to the age and gender of the affected patients at the time of diagnosis, as well as their anatomical distribution based on their clinical presentation, radiological features and histopathological examination. It is evident that the number and variety of cysts that can occur in the jaws are greater than those in any other part of the body[16]; consequently, dental practitioners must keep up with advances in this field, including the definition of new entities, methods of diagnosis and follow up patterns.

Materials And Methods

Cystic lesions diagnosed in both consecutive and referred patients, those seen at the department of Oral Medicine, Oral Pathology, Diagnosis and Radiology, Faculty of Dentistry; Garyounis University, Benghazi; in the period from January 1989 through to June, 2003. Only Libyan patients were included; their age, gender and area of residence were registered as well. For every patient, a detailed case history was obtained and specifically included the associating pain symptoms, site of the lesion and its duration. A comprehensive clinical examination was undertaken to elicit the lesion's clinical presentation, beside that; appropriate radiographs for all cases were taken to assess the radiological features of each of them. Biopsies of the intrabony cystic lesions including their linings and surrounding tissues were prepared by standard methods and stained with haematoxylin and eosin for histopathological examination under light microscope.
Retrieved data were tabulated and classified according to the new World Health Organization's classification for odontogenic tumors and cysts (Table1) and analyzed statistically to determine the frequency of jaw cysts in regard to the patient's gender and age at the time of diagnosis, as well as the site of predilection and the distribution of each cyst.

Table 1:
WHO classification of epithelial cysts of the jaws

Number	*Disease*	*ICD-O**
3	**Epithelial cysts**	
3.1	Developmental	
3.1.1	***Odontogenic***	
3.1.1.1	**"Gingival cysts" of infants (Epistein's pearls)**	26540
3.1.1.2	**Odontogenic keratocyst (primordial cyst)**	26530
3.1.1.3	**Dentigerous (follicular cyst)**	26560
3.1.1.4	**Eruption cyst**	265550
3.1.1.5	**Lateral periodontal cyst**	26520
3.1.1.6	**Gingival cysts of adults**	26540
3.1.1.7	**Glandular odontogenic cyst; sialo-odontogenic cyst**	26520
3.1.2	*Non-odnotogenic*	
3.1.2.1	**Nasopalatine duct (incisive canal)cyst**	26600
3.1.2.2	**Nasolabial (naso alveolar) Cyst**	26500
3.2	**Inflammatory**	
3.2.1	**Radicular cyst**	43800
3.2.1.1	**Apical and lateral**	
3.2.1.2	**Residual**	
3.2.2	**Paradental (inflammatory collateral, mandibular infected buccal) cyst**	26520

Morphology code of the International Classification of Diseases for Oncology (ICD-O) and the Systematized Nomenclature of Medicine (SNOMED). (Modified from Shear M, J Oral Pathol Med 1994;23:1-11).

Results

The study comprised 422 Libyan patients, their age ranged from 9 years through to 72 years, in which 264 (62.5%) of them were males and 158 (37.5%) were females at a ratio of 1.7 : 1. about 66% of cysts occurred in persons of less than 30 years of age (Table2). Two hundred and sixty one (61.8%) cysts occurred in maxilla, whilst 161 (38.2%) occurred in mandible. All cyst types occurred almost equally at either side of both jaws; and the most important clinical presentation was painless swelling at the site of involvement. The clinical and radiological findings in all the patients were confirmed by histopathological examination and revealed the diagnosis of apical (radicular) cyst in 306 (72.5%) patients, dentigerous (follicular) cyst in 60 (14.2%), odontogenic keratocyst (primordial) in 29 (6.8%), residual cyst in 14 (3.3%), nasopalatine duct cysts in 8 (1.9%) and lateral developmental periodontal cyst in 3 (0.7%) cases. Two (0.5%) pseudocysts were found in this study represented by aneurysmal bone cyst were found in the molar area of each jaw (Figure 1).
The anterior area of upper jaw contained about 37.6% of the total number of cysts, and the molar-ramus area of the lower jaw contained 24.6% of the cysts, whereas the premolar areas of both jaws contained only 14.6% of them. According to cyst type; the api-

cal (radicular) cysts tend to associate with upper front teeth (Figure 2a), while dentigerous (follicular) and odontogenic keratocysts (OKC) were most commonly seen in the body and angle or the ramus of mandible (Figures 3 & 5). All the residual cysts in this study (except one) occurred in maxilla with no age preferences. Four cases of mural ameloblastoma had developed in the walls of dentigerous cysts in female patients from this group of patients; all of them were located at the angle and ramus of the mandible (Table3).

Table 2: Distribution of jaw cysts according to Age groups

Age group (Years)	TYPE OF CYST														Total	Percent
	Odontogenic										Non odontogenic		Pseudocyst			
	Inflammatory				Developmental											
	Apical		Residual		Dentigerous		OKC		LPC		Nasoplatine		Aneurysmal bone			
Sex		*f*	*M*	*f*	*m*	*f*	*m*	*F*	*m*	*F*	*m*	*f*	*m*	*F*		
< 10	8	2	0	0	4	1	1	0	0	0	0	0	0	0	16	3.8%
10 - 19	49	37	2	1	11	6	4	5	0	0	0	1	0	2	118	27.9%
20 - 29	63	42	3	2	16	7	6	1	0	1	2	2	0	0	145	34.3%
30 - 39	32	16	0	1	4	4	3	0	1	0	0	0	0	0	61	14.4
40 - 49	19	12	1	1	2	1	2	3	0	0	0	0	0	0	41	9.7%
50 - 59	15	6	2	0	3	0	0	0	1	0	2	1	0	0	30	7.0%
60 & up	3	2	1	0	1	0	3	1	0	0	0	0	0	0	11	2.6%
Total	189	117	9	5	41	19	19	10	2	1	4	4	0	2	422	100%
	306		14		60		29		3		8		2		422	

OKC= odontogenic keratocyst; LPC= lateral periodontal cyst
Sex (M=male; F=female

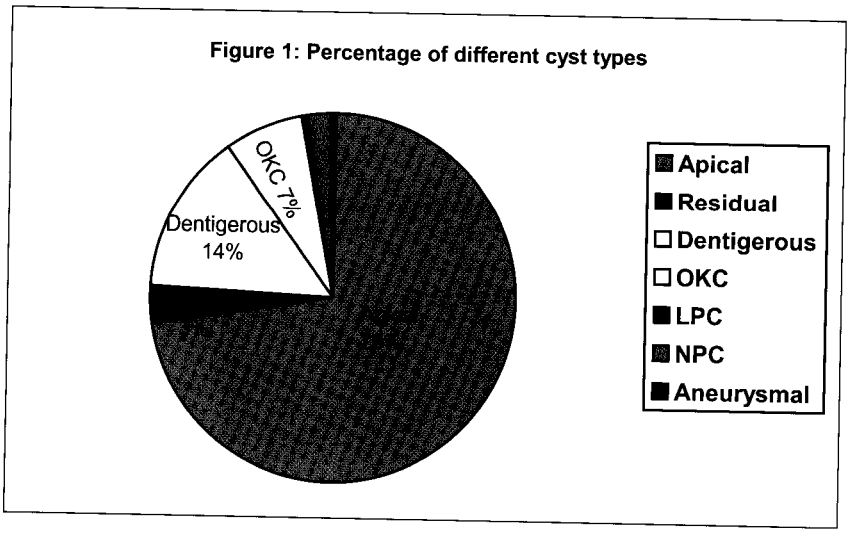
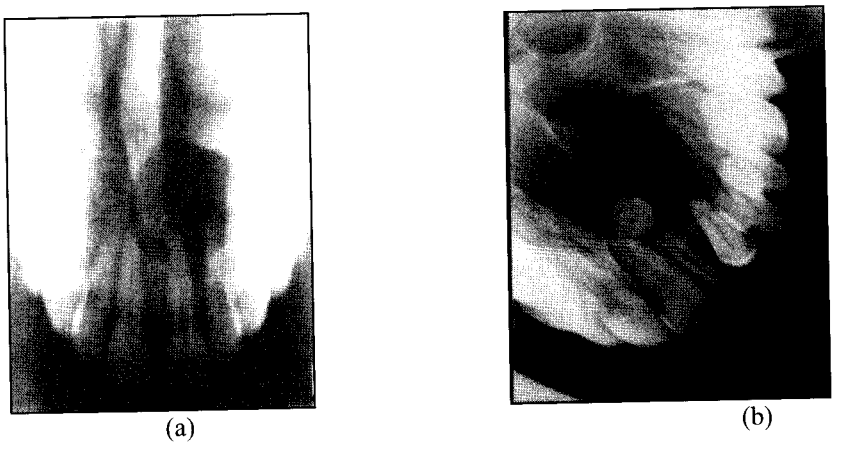


Table 3: Site distribution of jaw cyst in the age group

Site		Side	Type of cyst: Odontogenic: Inflammatory: Apical	Inflammatory: Res	Developmental: Deg	Developmental: OKC	Developmental: LPC	Non odontogenic: NP	Psuedo: Aneur	Total number: Side	Total number: Site	Total number: Jaw	Percent
Maxilla	Anterior	Rt	46	3	7	0	1	0	0	57	159	261	61.8 %
		Mid	33	2	6	0	0	8	0	49			
		Lt	38	1	9	5	0	0	0	53			
	Premolar	Rt	10	1	2	0	0	0	0	13	39		
		Lt	22	1	0	1	2	0	0	26			
	Molar	Rt	24	4	3	2	0	0	0	33	63		
		Lt	23	1	0	5	0	0	1	30			
Mandible	Anterior	Rt	3	0	0	0	0	0	0	3	34	161	38.2 %
		Mid	17	0	3	0	0	0	0	20			
		Lt	10	0	1	0	0	0	0	11			
	Premolar	Rt	8	1	1	0	0	0	0	10	23		
		Lt	10	0	0	3	0	0	0	13			
	Molar	Rt	30	0	15	5	0	0	1	51	97		
		Lt	32	0	9	5	0	0	0	46			
	Angle & Ramus	Rt	0	0	1	3	0	0	0	4	7		
		Lt	0	0	3	0	0	0	0	3			
Total number			306	14	60	29	3	8	2	422	422	422	100 %
Percent			72.5%	3.3%	14.2%	6.8%	0.7%	1.9%	0.5%	100.0%			

Res= Residual; Deg = Dentigerous; OKC = Odontogenic keratocyst; LPC = Lateral periodontal cyst; NP = Nasopalatine cyst; Aneur = Aneurysmal bone cyst.
Side (Rt = right; Lt = left; Mid = Middle)



(a) (b)

Figure 2:
(a): Large apical cyst at upper anterior teeth.
(b): dentigerous cyst associating with an impacted upper tooth

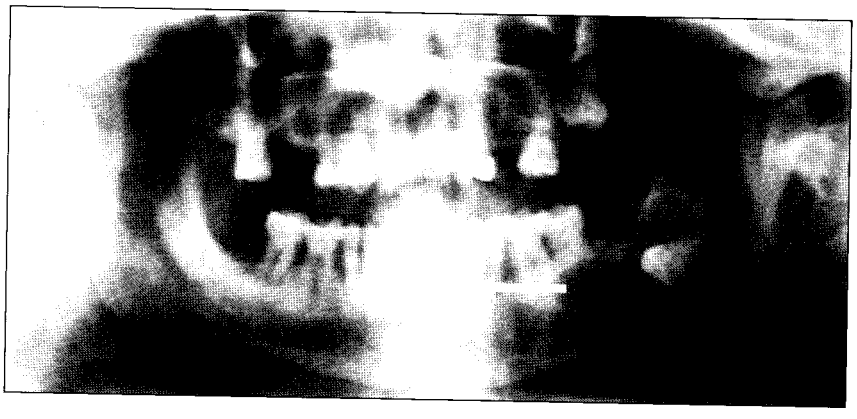


Figure 3: Radiological appearance of dentigerous cyst associated with an impacted wisdom tooth of 43 years old female

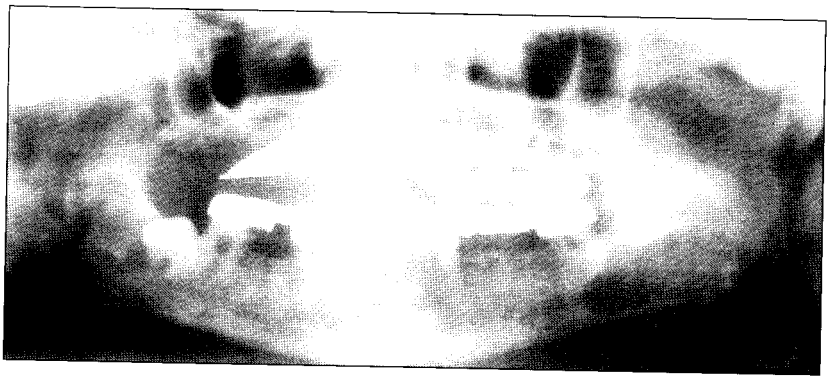


Figure 4: Bilateral Dentigerous cysts associating with impacted wisdom teeth.

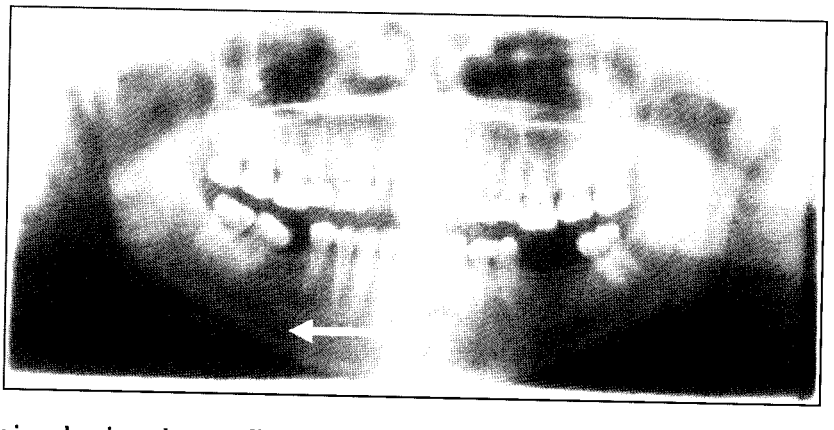


Figure 5: An OPG view showing a large radiolucency (arrow) apical to the lower incisors and left premolars of 22 years old female. The histopathological examination revealed an odontogenic keratocyst.

Discussion

This study is reporting frequency of intrabony jaw cysts, as they make up the majority of cysts in the maxillofacial region and their pathogenesis and clinical course is quite different from extraosseous cysts [4,17]. Present data revealed that the jaw cysts are more likely to occur in males rather than females, with an age distribution almost comparable with that of previous worldwide studies [3,8,17-19].

The frequency of different types of jaw cysts in our study (Table 2) is almost similar to previous studies of other populations[1,20] as the odontogenic inflammatory jaw cysts dominate other types. Previous studies concluded that radicular apical cyst make about 56% to 65% of intrabony jaw cysts, followed by dentigerous cyst in about 18% to 24%; the odontogenic keratocyst in 3% to 4% and the nasopalatine duct cyst makes about 2.5% to 2.7%,[1,18,21]. Whereas other types such as aneurysmal bone cyst and lateral periodontal cyst each makes less than 1% of jaw cysts [20]. Possibility exists of the bilateral occurrence of the same type of cyst or the simultaneous occurrence of more than one cyst type in the same patient[22,23]. It is noteworthy that the

reported variations in percentage of different types of cysts are in part due to the ever changing knowledge about jaw cysts including the emergence of some new entities, such as the glandular odontogenic cyst; and the deletion of the old incorrect concept of maxillofacial fissural cysts, including the globulo-maxillary cyst[16].

There have been some regional variations in regard to anatomical distribution of different types of jaw cysts in this study as it had been reported by other previous studies. It is generally agreed that the maxillary anterior region and the mandibular molar area were the sites of cystic preponderance[1,8,18]. Most jaw cysts have asymptomatic and prolonged course unless they are secondarily infected and seldom cause any noticeable neurological symptoms[12]. In this study pain symptoms were rare and few patients complained of pain symptoms. However, the most important clinical presentation was localized swelling of the involved area of variable duration.

The radiological appearance of the majority of jaw cysts is helpful in detection and follow up of their clinical course[24,25] nonetheless, an accurate diagnosis can not be solely drawn up from radiological features alone [26] and final diagnosis can only be ascertained by histopathological examination [8].

Radicular cyst (usually a consequence of pulpal necrosis) is the most common pathological periapical radiolucency[8,19,24,27] that are sometimes confused with other periapical pathosis[28]. It arises from proliferation of the epithelial rests of Malassez stimulated by inflammatory products from pulpal necrosis of the associated tooth, and enlarges by unicentric expansion from the hydrostatic pressure of its contents [5]. The most common location for such cysts is the maxillary anterior region, followed by maxillary posterior, mandibular posterior, then mandibular anterior areas without any age differences in this pattern of distribution A reduction of cyst size has been reported with increasing cyst age[29] and healing usually follows conventional root canal therapy of the (periapical pocket cyst) type[30], while the (true apical cyst) type is less likely to be resolved without surgical intervention[31].

Residual cyst is an inflammatory cyst that remains in the jaw after the tooth from which it originated is not present, either it may have exfoliated or it may have been removed surgically, this happens despite the fact that the majority of radicular cysts heal spontaneously following the loss or extraction of the associated tooth[32]. Such cystic lesions persist for a while, but most of them eventually undergo spontaneous slow resolution[29]. In this study, residual cysts seen in all age groups of both sexes, but most of them were in the anterior region of maxilla.

Dentigerous cyst has predilection to the mandibular ramus and molar region and usually associates with an impacted tooth[6]. It arises from pooling of inflammatory exudate derived from the obstructed follicular veins of an unerupted tooth and accumulates between the reduced enamel epithelium and the crown of the tooth and enlarges by unicentric expansion from the hydrostatic pressure of its contents[5]. It may accompany Maroteaux-Lamy syndrome (MPS VI), or contemporaneously exists with adenomatoid odontogenic tumor[33,34]. None of these conditions were reported in the present group of patients. Bilateral occurrence of dentigerous cysts has been reported previously[22,33] and there was one of such cases in our series of patients (Figure 4). This type of cysts can attain very large size with local destruction and expansion (Figure 3), but spontaneous regression has also been reported [22,35].

In few cases malignant changes such as mural ameloblastoma can arise in the wall of dentigerous cyst[14,15]. In our study malignant changes in the wall of dentigerous cyst in four females, but it has also been reported previously in males[6].

Odontogenic keratocyst presents an aggressive course with a tendency to recur following surgical treatment[36-38], it possibly have bimodal age distribution that peaks at second and sixth decades of life[39,40]. It arises by proliferation of the residues of the dental lamina and enlarges by both multicentric expansion due to the proliferation of localized groups of epithelial cells in their lining and by unicentric expansion from the hydrostatic pressure of its contents[5]. In this study this type of cysts occurred in relatively young persons of both sexes, and affected males as twice as females (Table 3). Most lesions occurred in molar and premolar areas of both jaws.

The clinical behavior of OKC frequently mimics that of benign tumors with displacement of teeth, resorption of the roots of teeth; "seeding" of the cyst into soft tissue and pathological fracture of the mandible exemplify this behavior[39]. Multiple OKCs are seen in Gorlin and Goltiz's syndrome with a proclivity for local invasion and recurrence[41,42]. Radiologically OKC is seen as unilocular or multilocular radiolucency of different sizes (Figure 5), commonly in the molar region of either jaw[43,44], thus, they may be mistaken for periapical lesions of endodontic origin[45]. Hard tissue deposits such as dystrophic calcifications, dentinoid and cartilage tissue all had been found in their wall [10].

The overall recurrence rate of OKCs ranges from 20% to 35%, and the average time to recurrence is 4 years[44], however, in recent years there had been reported decline in that rate due to better understanding of its behavior and consequent modifications of operative procedure employed in their treatment[6,46]. No information available regarding the recurrence rate of our 29 patients with OKC. Carcinomatous and ameloblastomatous transformation in OKC seems to be an extremely rare phenomenon and no case of such malignant change was detected in our series of patients[11,47].

Lateral developmental periodontal cyst is rather infrequently reported odontogenic cyst and seems to develop in direct contact to the periodontal membrane of an erupted vital tooth sharing some clinical and morphologic similarities to the gingival cyst of the adult[48]. Its incidence in this study is similar to those of previ-

ous studies as it accounted for only 0.7% of all jaw cysts[49,50]. Published reports have indicated that they occur most frequently in the 5th to 7th decades in the mandibular molar and premolar areas[6], in our study the subjects are of younger age and all cysts appeared in the premolar-incisor areas of maxilla seen as asymptomatic, small, ovoid, well- corticated radiolucency on interradicular locus of the roots, with mild degree of cortical expansion but without any perforation. The terms (botryoid odontogenic cyst) and (lateral periodontal cyst) have both been used to describe a histologically distinct type of odontogenic cyst characterized by a thin epithelial lining exhibiting focal thickenings or plaques[51]. The final diagnosis is to be established on a histological basis in conjunction with the clinical and radiographic findings to differentiate it from otherwise more aggressive lesions with similar appearance[52].

Nasopalatine duct cyst is thought to originate from epithelial remainants of the nasopalatine duct and is usually situated in the midline near the incisive canal, just behind the maxillary central incisors[53]. They are usually asymptomatic and limited in size, but they can cause plugging in the palate, or misdiagnosed with other cystic lesions[54]. They make up to 1.7% of all jaw cysts, with no age or sex predilections[18,21,53]. Eight (1.9%) cases have been diagnosed in this series of patients at different ages and equally distributed in both sexes.

The origin and pathogenesis of aneurysmal bone cyst is under intense debate, but it is widely known that this mysterious condition affects young persons under the age of 20 years, with no significant predilection for either sex[55]. It is generally agreed that the mandible is affected more frequently than the maxilla[56], and usually presents as painful swelling that sometimes causes tooth mobility[57]. The radiographic picture consists of an eccentrically ballooned and expanded cystic boney lesion with a honeycomb or soap-bubble appearance. Characteristically, at the time of operation, a common finding is the "welling up" of blood from tissue that resembles blood-soaked sponge[55]. In the present study two cases of aneurysmal bone cysts were found in young females at their molar area of either jaw, however, there was no history of traumatic injury preceding the development of the lesion and no tenderness of the affected area, as it has been indicated in some previous reports[56].

Further studies are needed to explore the risk factors, predisposing factors and recurrence rate for each cyst type. Furthermore, the response to different treatment procedures is to be carefully assessed in view of the reported decline in recurrence rate of most types of jaw cysts, especially of the odontogenic keratocyst by adopting and employing new operative procedures.

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Histological Study of the Effect of Ibuprofen on Rat Kidney

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الملخص

انتشر استعمال الأدوية اللاستيرودية مثل الايبوبروفين كمضاد للالتهاب ومسكن الألم منذ أكثر من 30 سنة مضت. في السنوات الأخيرة هناك العديد من التقارير التي تفيد بأن هناك علاقة بين أمراض الكلى واستخدام ايبوبروفين لذلك كان الغرض من هذه الدراسة هو ملاحظة التغير النسيجي في الكلى واستخدام ايبوبروفين. بعد إعطاء الدواء والجرعة المفرطة عن طريق الفم وبعد وقف الدواء. تم استخدام ٨٤ فأر قسمت إلى أربع مجموعات، مجموعة تحكم ومجموعة استقبلت العلاج من ايبوبروفين يومياً والأخرى استقبلت جرعة مفرطة والمجموعة الأخيرة تركت.. **الطريقة**: بارا فين، صبغ روتيني، أصباغ خاصة وتقنية كيمياء النسيج. **النتيجة**: الاستخدام الطويل لعلاج ايبوبروفين والجرعة المفرطة لمدة قصيرة بينت درجات متفاوتة من التغيرات النسيجية. ازدياد ترسب الكولاجين لوحظ حول العديد من أنابيب الكلى. التغيرات في الأنابيب والجدار القاعدي للكبيبة. التوقف عن الدواء لا يؤدى إلى الشفاء الكامل. **الاستنتاج**: استخدام ايبوبروفين لفترة طويلة أو أخذ جرعة مفرطة منه يتسبب في درجات متفاوتة من الضرر الكلوي والشفاء منه ليس تاماً بعد التوقف عن الدواء.

Abstract

Objectives non-steroid anti-inflammatory drugs such as ibuprofen has been in wide spread use as anti-inflammatory & analgesics for more than 30 years and has been introduced as over the counter drugin many countries. In recent years there has been an increasing number of reports of various types ofrenal diseases that are associated with long-term therapeutic doses of ibuprofen. Not much work has been done on the histological changes accompanying the use of ibuprofen in animals. Thus the aim of thiswork is to study the histological changes in rat kidney after administration of therapeutic & overdoses of ibuprofen orally. **Material & Methods:** eighty four male albino rats were used & divided into four groups, one used as control group, one received therapeutic dose of ibuprofen daily, one received overdose and the last group was left for recovery. Paraffin, routine stain, special stains & histochemical technique were used in this study. **Results:** the results indicate that **1**. Long treatment of therapeutic doses& short treatment of overdoses of ibuprofen showed variable degrees of histological changes predominantly within the interstitial tissue ranging from marked interstitial cellular infiltrates to focal degenerative fibrotic areas. **2**. Increased deposition of collagen fibers was detected around many renal tubules, renal corpuscles and renal Arterioles. **3**. Changes in tubular and glomerular basement membrane were also detected. **4**.Discontinuation of the drug does not lead to complete recovery. **Conclusion:** ibuprofen when taken in overdoses or taken in therapeutic doses for long time causes variable degrees of renal injuries and the recovery was incomplete after discontinuation of the drug.

Introduction

Inflammatory disease are widely spread today among a great variation of population. A lot of anti inflammatory drugs are used for different diseases and for variable periods[1]. Ibuprofen is one of these drugs which is commonly used as analgesic and as anti inflammatory drugs in humans since 1967 in England and 1974 in the United States[2]. It is well known that ibuprofen as well as all other non-steroidal anti-inflammatory drugs may cause a number renal side effects especially when its used for a long time or in large doses [2,3].

The drug is considered safe in human[4] but there are many reports of ibuprofen associated nephrotoxicity, including reduction in renal function, acute renal failure, interstitial nephritis and papillary necrosis.[5,6,7] in addition to thickening of the wall of capillaries in the sub-mucosa of the renal pelvis[8]. In recent years there has been an increasing number of reports of various types of renal diseases that are associated with short-term therapeutic doses of ibuprofen[7] . No much work has been done on the histological changes accompanying the use of ibuprofen in animals. It was thuds decided to study the histological changes in rat kidney as it is the main parenchymatous organ responsible for its excretion and to examine the validity of using animal models to provide a deeper understanding of its possible toxicity in human as a step to evaluate its safety. The present paper describes:

1. The histological changes in rat kidney after oral administration of therapeutic and overdose of ibuprofen.
2. The histological changes after discontinuation of the drug.

Materials and Methods

Animals

The rat used in this study were obtained from the animal house Faculty of Medicine, Garyounis University, Benghazi, Libya.

Materials

Ibuoprofen syrup was obtained from Boots Company, PLC, Nottingham, England. All other chemical were of A.R grade and obtained from Commercial Suppliers.

Treatment of animals with Ibuprofen:

Eighty four (84) male albino rats weighing (260-320gm) were used in this study. The animals were divided in to four groups. Group -I- received normal saline orally (Table I) using the original flexible silk rubber tube with a syringe needle head and considered as a sham control for this experiment[9]. Group-II- received daily therapeutic dose of ibuprofen orally and subdivided into four subgroups (Table II). The dose was adjusted for rats according to the

formula of Pagat & Barnus[10] and of TvrZicka,[11]. Group III- received daily overdose of ibuprofen orally and subdivided into four sub-groups identical to that of group-II- (Table II). Group-IV-, represent the recovery group and subdivided into two sub-groups, one received daily therapeutic dose and the other one received overdose of ibuprofen for four weeks. Then the drug was discontinued and the animals were left for recovery for 14 & 28 days for both doses (Table II).

Histological Studies

All the animals were sacrificed by the last dose of each period. Both kidneys were excised from each animal and fixed 10% formol saline for preparation of paraffin sections.

Preparation of paraffin sections: The specimen were processed according to Culling et al[12]

Routine staining technique with Hematoxylin & Eosin (H&E) was used as a routine technique in histology and routine pathology[13].

Special staining with Heidenhains (Azan) stain was used to demonstrate the distribution of connective tissue[14].

Periodic Acid-Schiffs (PAS) reaction technique [12] was used to demonstrate the PAS positive materials such as complex carbohydrates that exist in the basement membrane.

Results

Animals received normal saline

Hematoxylin and Eosin (H&E) stained sections showed typical morphological picture of normal kidney parenchyma & papilla (Fig 1 a, b). The other special stains (Azan &Pas) showed normal distribution of collagen fibers in the interstitial connective tissue (Fig. 1c, d) and normal thickness of basement membrane respectively.

Animals receiving therapeutic doses of ibubrofen

Sections stained with (H&E) showed variable degrees (mild-marked) increase of interstitial infiltrates of lymphocytes, plasma cells, eosinophils, macrophages and occasional neutrophils, in both cortex and medulla (Fig 2a). The urothelium of the pelvic region also showed moderate to marked increase of cellular infiltrates predominantly esinophils. Some dilated renal tubules filled with esinophilic material were also observed in the cortex (Fig 2,b) while the renal glomeruli & most of the renal tubules appeared to be well observed. Marked increase of collagen fibers was observed around many of the renal tubules as well as in the sub-mucosa of the renal pelvis after three weeks of daily intake of ibuprofen (Fig 2c, d) while the tubular and glomerular basement membrane showed decrease in the PAS-positive material.

Animals receiving overdoses of ibuprofen

Small focal degenerative fibrotic areas with dilated tubule (Fig 3a) and many dense areas of cellular infiltrates were seen in the renal cortex after one week of daily intake of ibuprofen overdose.

Multiple hemorrhage areas were also observed in the cortex and cortico-medullary junction (Fig 3b). Regarding the collagen distribution, dense deposition of collagen fibers was observed in the fibrotic areas (Fig 3c), around the hemorrhagic areas as well as around many renal tubules (Fig 3, d). Sections after three and four weeks of overdose intake showed an apparent hyperplastic region at the apex of the renal papilla with many mitotic figures (Fig 3 e, f).

Recover animals

The renal cortex of the rats that received therapeutic doses of ibuprofen and left for recovery for two and four weeks showed separate tubules and edematous interstitial tissue. Many of the lining epithelial cells of these renal tubules showed vacuolated cytoplasm (Fig 4 a). The renal tissue also showed dense collagenous fibers around many renal tubules and renal corpuscles. In addition an increase in the thickening of tubular and glomerular basement membrane was observed.

Animals that received overdoses and left for recovery for two weeks showed many collecting tubules filled with eosinophilic material. Many mitotic figures were seen among the lining cells of collecting tubules in both medulla and papilla. In addition many small hemorrhagic and dense inflammatory areas were also observed. On the other hand large homogenous acidophilic area with loss of many collecting tubules and dilating of others was observed in the renal papilla after four weeks of recovery (Fig 4b). Hyperplastic epithelial changes with many mitotic figures has been shown in some region of the papilla (Fig 4c, d) while the tip of the papilla showed large ring-shaped projection with central cavity and eosinophilic material filled the wall of the ring (Fig 4b).

Table I* - Animals received normal saline						
Animal Subgroup	No. of Animals	Dose of Saline ml/kg/day	Period of treatment	No. of animals taken 24 hrs. after last dose	Period of recovery after last dose	No. of Animals taken during recovery
SGA	12	3.5	7, 14, 21 and 28 days	3 at each period	_____	_____
SGB*	6	3.5	28 days	_____	14, 28 days	3 at each period
SGC	12	7.0	7, 14, 21, and 28 days	3 at each period	_____	_____
SGD*	6	7.0	28 days	_____	14, 28 days	3 at each period

***SGA and SGB: Animals received single dose.**
***SGC and SGD: Animals received double dose**
*** SGB and SGD: Recovery groups**

Table II: Group II* and Group III** - Animals received Ibuprofen						
Animal Subgroup	No. of Animals	Dose of ibuprofen mg/kg/day	Period of treatment	No. of animals taken 24 hrs. after last dose	Period of recovery after last dose	No. of Animals taken during recovery
SGA	16	6mg	7, 14, 21, 28 Days	4 at each period	_____	_____
SGB*	8	6mg	28 days	_____	14, 28 days	4 at each period
SGC	16	12 mg	7, 14, 21, 28 days	4 at each period	_____	_____
SGD*	8	12 mg	28 days	_____	14, 28 days	4 at each period

***SGA and SGB: Animals received therapeutic dose.**
***SGC and SGD: Animals received overdose**
***SGB and SGD: recovery groups**

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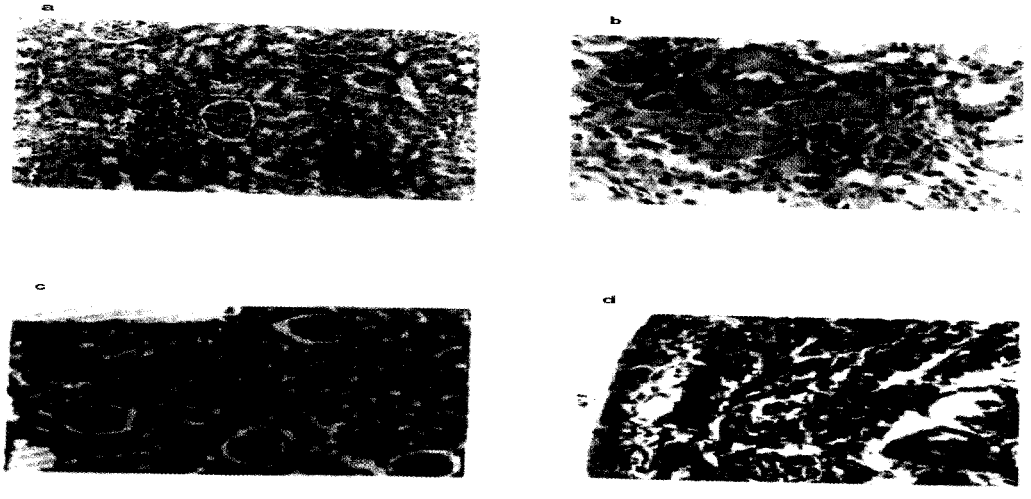

Fig 1: Animals recevied normal saline
- a- normal structure of kidney cortex.
- b- normal structure of papilla & renal pelvis. B & c & d – normal distribution of collagen fibers.

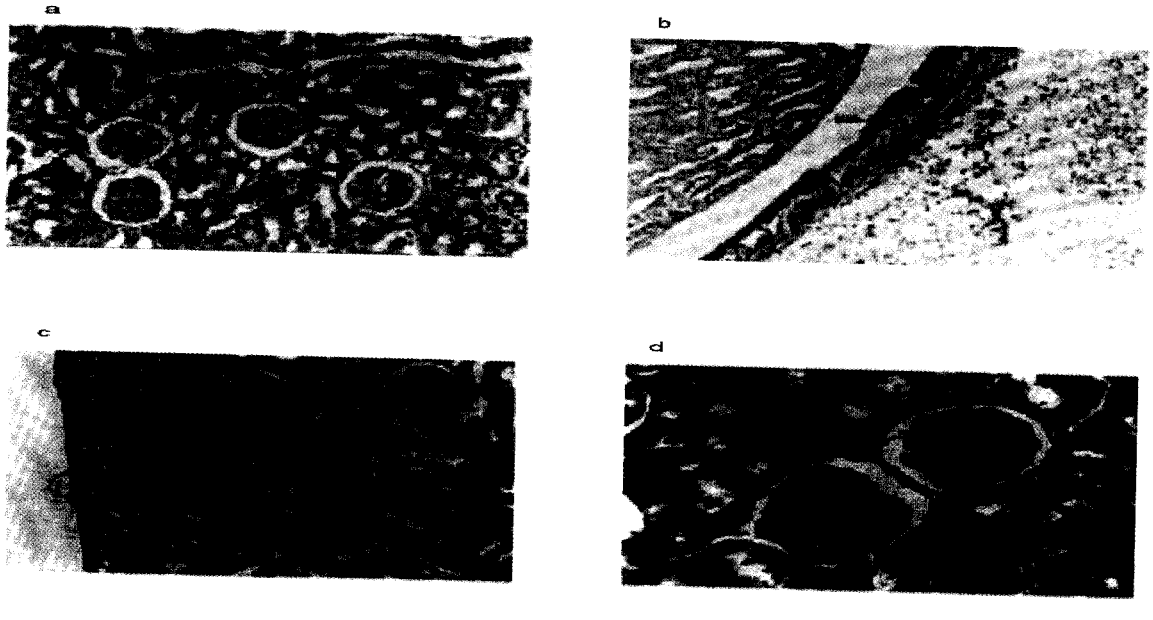

Fig 2: Animals received therapeutic doses of ibuprofen
a- kidney cortex with cellular infiltrates.
b- renal tubules filled with eosinophilic materials and congested blood vessels.
c- increased deposition of collagen fibers in kidney cortex.
d- increased deposition of collagen fibers in the urothelium at the pelvic region.

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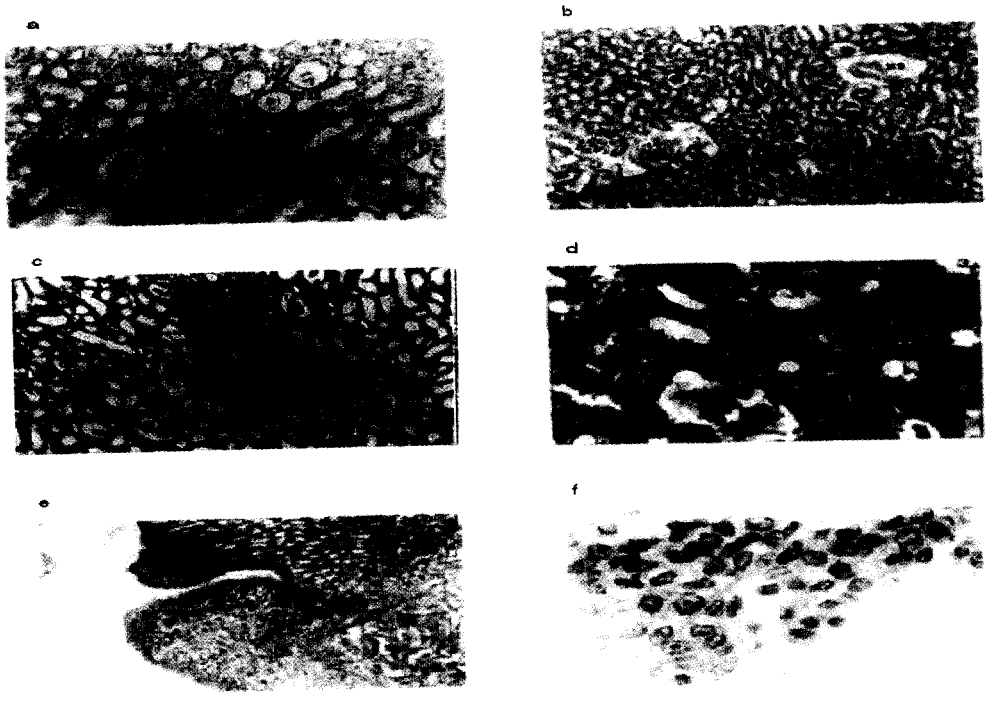

Fig. 3: Animals receiving overdoses of ibuprofen

- **a) renal cortex with degenerative fibrotic area.**
- **b) renal cortex with multiple hemorrhagic Areas.**
- **c) the degenerative fibrotic area showing the deposition of collagen fibers.**
- **d) Increased deposition of collagen fibers around many renal tubules.**
- **e) apex of renal papilla.**
- **f) With hyperplastic regions.**
- **g) the hyperplastic region with many mitotic figures.**

Discussion

Ibuprofen is a propionic acid derivatives with anti-inflammatory, antipyretic & analgesic properties. It represent a valuable tool in the medical therapy of rheumatic disease and for this reason its wide spread use is understandable [15,16].

The appropriate of animal models offers very important key to understand the pathomechanism of renal papillary necrosis and to provide a model system to improve the early diagnosis of the lesion and to identify which analgesic (S) has the greatest papillotoxic potential.

Histological findings

I. Animals receiving therapeutic doses of ibuprofen: It is well known that ibuprofen as well as other non steroid anti inflammatory drugs has analgesic effects in low doses (0.2-0.8g/day) with anti-inflammatory effects becoming clinically apparent at high, more prolonged dosage (<1.6g/day) and maximum dose should not be more than (0.8g/day) for limited number of days only [3,17,18]. In this group of animals, the renal injuries were variable and the interstitial tissue exhibited the important changes. The interstitial cellular infiltrates that were observed in variable densities in both cortex and cortico-medullary junction consisted predominantly of lymphocytes, but plasma cells, eosinophils, neutrophils and macrophages were also prominent. These cells are commonly found, infiltrating the tissue as part of chronic inflammation process [19]. Increase in cellular infiltration was also detected in the sub-mucosa of urothelium at the pelvic region with prominent high number of eosinophils. Accordingly it can be suggested that the long-term treatment of therapeutic doses of the drug can affect the urothelium and may consequently induce either a classic allergic reaction as many eosinophils present, or may be related to a direct drug-induced effect on urothelium itself with secondary activation of

lymphocytes [15]. It is generally accepted that long-term treatment with therapeutic doses of ibuprofen represent an important cause of interstitial nephritis[2, 3] and changes on renal tubules have been reported in most cases of interstitial nephritis[20]. This is true as regarding this work since the appearance of renal tubules in both cortex and cortico-medullary region was variable including dilation of some tubules with flattened epithelial cells and others with eosinophilic material in their lumens. Theses findings are in accordance with that obtained by codding[21] et al and Dixon[22].

Congestion of blood capillaries with interstitial hemorrhages may be due to the rupture of the endothelial wall of greatly dilated capillaries, causing bleeding into the interstitial tissue [16]. The increased deposition of collagen fibers which was observed around many renal tubules, glomeruli and blood vessels may be attributed to the stimulation of fibroblast-like cells (type I interstitial cells) resulting in an increased synthesis of collagen fibers[23, 24]. The decrease in the PAS positive material that was detected in the tubular and glomerular basement membrane was in agreement with that found by Cohen & Hoyer[25] and Olsen etal[26]. They demonstrated that there were constant morphological alterations affecting both tubular and glomerular basement membrane due to drug associated acute interstitial nephritis. These changes include extreme thinning and attenuation of the basement membrane which may be due to the migration of lymphocytes through the tubular basement membrane.

Animals receiving overdoses

One week following daily overdose intake of the drug, the focal degenerative fibrotic areas found in the cortex were the most distinct feature in addition to other interstitial changes mentioned above. These findings are similar to those reported by many workers[20,27,28]. They demonstrated that variable degrees of interstitial fibrosis, tubular atrophy and tubular loss and arterioles thickening are the morphological features associated with an ibuprofen overdose treatment. The underlying mechanisms producing such lesion are not understood[22]. It seems that a variety of initial insults may give a rise to similar histological appearance including ischemia, immunological reaction, infection and obstruction of urine outflow. It is well known that repeated intake of ibuprofen overdoses results in renal papillary necrosis and with the process of the disease, the tissue at the tip of the papilla become necrotic and small or large fragments are shed and the raw area then re-epithelized[29, 30]. This might explain the hyperplastic epithelial tissue observed in this study after three weeks of overdoses.

III-Recovery groups

Animals receiving therapeutic doses

The persistence of dense cellular infiltration, vascular-wall thickening, edematous cortical interstitial tissue with separated tubules are principle findings seen in the animals after 14& 28 days of recovery. In addition, cytoplasmic vacuolation of tubular epithelial cells dense distribution of collagen fibers were noticed focally. It has been shown that vacuolation & glycogen accumulation in epithelial cells of distal and collecting tubules may represent a response to intracellular accumulation of the drug such as with lithium therapy[31]. It is also shown that vacuolization of the cells of the straight part of proximal tubules is due to dilatation of smooth & rough endoplasmicreticulum[8] All these findings are parallel to those found in many which indicates that the risk of ibuprofen associated nephrotoxicity is exceedingly small and is unlikely to follow short-term therapeutic dose of ibuprofen in man[17] or in rat[29]. It is well known that withdrawal of ibuprofen usually leads to recovery and the return to the baseline function was gradual and may takes as long as few weeks to several months and it may be incomplete[32,33]

Animals receiving overdoses

Detailed study of recovery animals of this group showed progressive alteration of papillary architecture after 14 days of recovery while after 28 days the incidence of papillary necrosis was more advanced with complete alteration of papillary architecture. These changes are parallel to those reported by other investigators[7,29]. They demonstrated that ingestion of large quantities of non-steroidal anti-inflammatory drugs including ibuprofen or combination of analgesics initially affects the papilla and the inner medulla and consequently leads to papillary necrosis. The presence of large ring-shaped projections from the tip of the papilla with a large central cavity may be related to that found by Lindvall[34]. He showed that the presence of medullary or papillary cavities or the presence of rings of calcification around the necrotic papilla may be demonstrated by radiology. It has been shown that successful histopathological identification of the lesion needs careful attention to cutting serial sections to find the papillary apex since histopathology may miss focal lesions and often an apex-limitd lesion undergoes abscission from the rest of the medulla[29]. The mitotic figures seen among the lining epithelium of dilated collecting tubules in both medulla and papilla and the mitotic figures seen among the hyperplastic epithelial tissue at the necrotic papilla may be considered as an indicator of regression. Damage to the tubular epithelial cells with evidence of regeneration is always found in association with drug-induced acute allergic tubulo-interstitial nephritis while evidence for regeneration with mitosis in epithelial cells has also been reported[35,22]. The mechanism of papillary necrosis is far from clear. One possible explanation is that there is an interference with blood supply to the papilla[36]. They demonstrated a reduction in medullary blood flow in an experimental study of analgesic nephropathy. The fact that non-steroidal anti-inflammatory drugs inhibit prostaglandin synthesis and diminish medullary blood flow suggests that these agents have the potential to

induce papillary ischemia[37]. Another possible explanation is that one or more of the chemicals in the analgesic compound directly damage the cells of the renal papilla[38].

Conclusions and recommendations

1- The ibuprofen when taken in overdoses or after long term intake of therapeutic doses causes variable degrees of renal injury and may lead to renal papillary necrosis.
2- The recovery may be incomplete.
3- The ibuprofen must not be an over -counter drug.
4- The physicians must take extreme caution when prescribing ibuprofen to patients with renal insufficiency.

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The Effects of Different Temperatures on the Growth of Plasmodium Falciparum

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الملخص

مقدمة: إن التوصل إلى طريقة زراعة الملاريا في المختبر تعتبر مطلبا أساسيا لدراسة ظروف ونمو المتصورة المنجلية.**الهدف:** تحديد تأثير درجات الحرارة المختلفة على نموها **الطريقة** تمت الزراعة في وسط RPMI مع 10% مصل بشرى في درجات حرارة متبادلة بين 37 و 40 درجة مئوية. **النتائج:** بينت الدراسة حدوث تكيف للطفيل مع تغيرات درجة الحرارة وتحوله إلى الطور الأكثر مقاومة. **الاستنتاج:** الاستعمال المتبادل لدرجة حرارة 37 و 40 يزيد من أعداد طفيل الملاريا وقد تكون هذه الطريقة هي الأحسن لزراعته في المختبر.

Abstract

Background: The establishment of a method for the in-vitro cultivation of malaria parasite was a prerequisite for research on the development and growth conditions of Plasmodium falciparum. **Objectives:** The present work was aimed to determine the influence of different and alternate temperature changes on the growth of P. falciparum. **Materials & Methods:** Parasites of the NF-54- and R-strain were cultured in RPMI-1640 medium with 10% human serum. In a first set of experiments the R-strain was cultured at two different temperatures (37°C and 40°C) for 4 days and the parasitemia was determined by blood smear examination every two days. In a second series of experiments the NF-54-strain was cultured at daily temperature changes of 37°C and 40°C for 16 days. **Results:** At 37 °C the parasitemia increased constantly until the fourth day to a value of 6.6%. At 40 °C the parasitemia decreased continuously reaching 0.2% at the last day of experiment. In spite of fluctuation of parasitemia during the first days of cultivation a slow but steady parasite increase was observed reaching 13.7% on the 12th day. However, on the 16th day the parasitemia decreased to 2%. The results obtained shows that alteration of temperature resulted in an adaptation of the parasite by the conversion to a more heat-resistant stage of the gametocyte. **Conclusion:** the use of alternate temperatures (37°C and 40°C) increases the yield of malarial parasite and it might be a better method for its cultivation in-vitro.

Keywords: Malaria, Plasmodium, NF-54-strain, Parasitemia.

Introduction

Plasmodium falciparum is the causative agent of malaria, a common infectious disease in tropical countries with high rates of morbidity and mortality. The search for an effective vaccine against malaria has started many years ago. Cultivation of the causative parasite in-vitro was an important step towards this goal. The establishment of a method for the in-vitro cultivation of malaria parasite was a prerequisite for research on the development and growth conditions of Plasmodium falciparum. The cultures offer the chance to investigate numerous problems related to genetic, biochemical, immunological and chemotherapeutical issues that cannot be examined in-vivo. Bass and Johns[1] were the first to try cultivation of P. falciparum and P. vivax in-vitro. They were successful only for a few developmental cycles at a temperature of 40°C corresponding to a feverish situation. Thompson and McLellan[2] repeated Bass and Johns experiments at a cultivation temperature of 38°C but they only achieved a short-term growth as well. During their development of the protocol for the continuous culture of P. falciparum, that is now a standard method, Trager and Jensen[3] finally defined the temperature as 37°C.

Any improvement in the yield of the cultivation methods used at present time to culture P. falciparum is important. However, using alternate temperatures for continuous culturing of the parasite had not been reported previously. Therefore, the aim of the present work was to determine the influence of different and alternate temperature changes on the growth of P. falciparum.

Materials and Methods

Parasites of the NF-54- and R-strain (as control) were cultured in 25mm Petri dishes according to Trager and Jensen[3]. Following the standard protocol, basic culture medium contained RPMI 1640 with glutamin, 50mg/l hypoxanthin, 0.2% NaHCO3 and 25m HEPES buffer was used. The pH adjusted to 7.0 by the addition of 1M NaOH. To complete the medium human serum was added to a concentration of 10%. The medium changed daily in all experiments.

In a first set of experiments, the R-strain was cultured at 37°C and 40°C for 4 days. In a second series of experiments, the NF-54-strain was cultured at daily temperature changes of 37°C and 40°C for 16 days. In all experiments parasitemia was determined by daily blood smear examination.

Results

In the first set of experiments, at a cultivation temperature of 37°C the parasitemia increased

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constantly until the 4th day to reach a value of 6.6% (Fig 1).
At 40°C the parasitemia had its maximum already on the 1st day with 1.6% and decreased to 0.2% on the last day of the experiment (Fig 1).

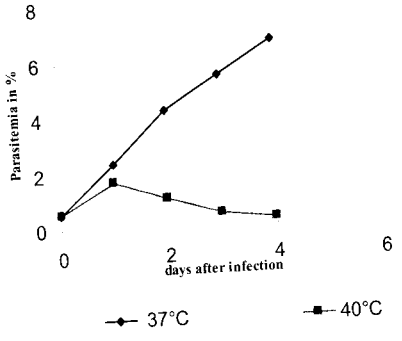

Fig:1 Parasitemia of a P. Falciparum culture (R-strain) after incubation at 37°C and 40°C for a period of four days.

Although most of the asexual stages seemed to be morphologically damaged on the 4th day at 40°C, they were in fact partially still viable and able to multiply as shown by an increasing parasitemia after another few days of cultivation at a temperature of 37°C (data not presented).
In the second series of experiments, and in spite of fluctuations of parasitemia during the first days of cultivation, a slow but steady parasite increase up to 13.7% at the 12th day (Fig 2a).
However, on the 16th day the parasitemia decreased to 2%. Furthermore, the gametocytemia of the cultures increased from the beginning of day 4 of cultivation to 3.2% on the 16th day of the experiment (Fig 2b).
To check the vitality of the parasites, cultures supplemented by fresh erythrocytes at the end of the experiment and incubated at 37°C. Consequently, a clear and fast multiplication of the parasites was observed (not evaluated quantitatively) and the developmental stages seemed to be morphologically intact.

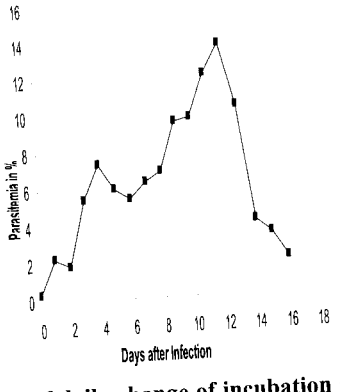

Fig: 2a Effect of daily change of incubation at 37°C (odd days) and 40°C (even days) on the parasitemia of P. falciparum NF54-strain.

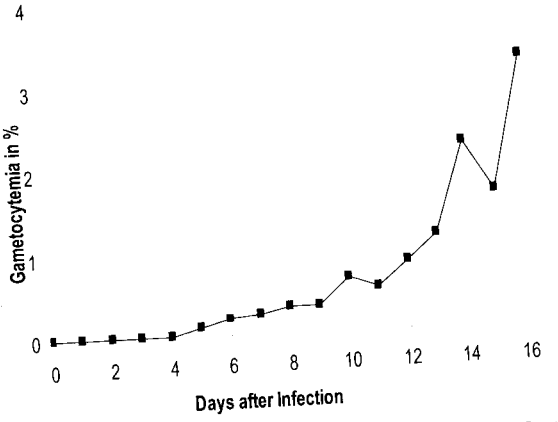

Fig:2b Effect of daily change of the incubation temperature between 37 and 40°C on the gametocytemia of P. falciparum, NF54-strain (the temperature was 40°C on the even marked days, 37°C on the uneven days, not marked).

Discussion

In a preliminary experiment of the work presented here the effect of different temperatures (37°C and 40°C) that are reached during a plasmodial infection on the vitality and the growth of the erythrocytic stages of P. falciparum were investigated in-vitro. The cultures that incubated at a constant temperature of 37°C showed a better parasite growth than the cultures incubated at 40°C. A temperature of 37°C corresponds to the normal body temperature to which the parasites seem to be adapted. In contrast, the cultures incubated at a constant temperature of 40°C, on the 4th day of the experiments and only had a parasitemia of 0.2%. Accordingly, the higher temperature obviously led to an inhibition of parasite development.
In a second series of tests, the effect of a daily change of temperature between 37°C and 40°C on the parasite growth was investigated in order to imitate the in vivo conditions during a typical intermittent fever. Although most of the parasites were still viable after the heat shock, their further growth slowed down. In blood smears only young trophozoites and schizonts were found but older ones not at all. Such temperature-associated processes are conceivable as a cause for the synchronization of the parasite growth in vivo. This is in agreement with the opinion of Gravenor et al[4]. that a typical fever attack during the primary infection of a non-resistant host by P. falciparum may result in a density-dependent regulation of the parasite population and thus can cause cyclic parasitemia episodes and lead to synchronous parasite growth.
After such an episode of fever, it is advisable for the parasite to leave the endangered host. From a biological point of view, a conversion to the transmissible stage of the gametocyte therefore makes more sense than a further cyclic multiplication during the erythrocytic phase. The demonstrated increase in the number of gametocytes after raising the cultivation temperature in the experiments of this work seems to confirm this phenomenon. The transformation into the

gametocyte stage could be triggered by the expression of special stress proteins as in the case of leishmania where a heat-shock-protein participates in the change of promatigotes to the infectious amastigote stage 5. For P. falciparum the production of specific stress proteins was demonstrated as a reaction to a heat stimulus as well[6], among them the heat-shock-protein PFHSP70-I 7-10 that possibly protects the parasite from heat death by taking part in the conversion into a more heat-resistant and transmissible stage[11]. The exact function of this protein, however, is still unknown[6,12,13]. In conclusion, the present work shows that the use of alternate temperatures (37°C and 40°C) increases the yield of malarial parasite and it might be a better method for its cultivation in-vitro.

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Indications and Complications of Caesarean Section at Jamahiriya Hospital, Benghazi

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الملخص

الهدف: دراسة راجعه لتقييم معدل العمليات الجراحية ومضاعفاتها في مستشفى الجماهيرية بنغازي- ليبيا خلال فترة ثلاث سنوات مضت 1998 - 2000 شملت الدراسة كل حالات الولادة عن طريق العمليات القيصرية (الاختياري والطارئ). **الطريقة:** جُمعت البيانات من ملفات المرضى من قسم الإحصاء بالمستشفى. المجموع الكلي للولادات في تلك الفترة بلغ 46467 حالة ولادة منها 5403 عن طريق العمليات القيصرية مثلت نسبة 11.6% . السبب الرئيسي للعمليات القيصرية الطارئة كان اختناق الجنين بمعدل 18.36% ، العمليات القيصرية الاختيارية 16.93% . السبب الرئيسي للمضاعفات كان التهاب الجرح 2.27% . **الاستنتاج:** نستنتج من الدراسة إن هناك ارتفاع في معدل العمليات القيصرية بمستشفى الجماهيرية ونتصح بالعناية بالأم قبل وأثناء وبعد فترة الحمل و كذلك تنظيم النسل قد يخفض نسبة العمليات القيصرية في مستشفياتنا مستقبلا.

Abstract

Objectives: To evaluate the rate, indications and complications of caesarean section at Jamahiriya Hospital in Benghazi Libya over 3 years (1998- 2000). **Materials and methods:** Retrospective study included all cases delivered by caesarean section. **Results:** The total number of deliveries over the period of the study was 46467 deliveries. 5403 cases were delivered by caesarean section. The rate of caesarean section was 11.6 %. The most common indication was foetal distress (18.36%) in cases of emergency caesarean section while repeated scar (16.93) in cases of elective caesarean section. Overall, the most common complication was wound infection 2.27%. **Conclusions:** Compared to previous reports, the caesarean section rate at Al-Jamahiriya hospital continues to rise and our findings were generally comparable to those reported elsewhere.

Introduction

Caesarean section denotes the delivery of the foetus, placenta, and membranes through an incision in the abdominal and uterine walls.

The first caesarean section performed on a patient is known as primary caesarean section, subsequent procedures are referred to as secondary, tertiary, and so on, or simply as a repeat caesarean section.

An elective caesarean section is performed before the onset of labour or before the appearance of any complication that might constitute an urgent indication.

Caesarean section could be classical in which the uterine incision is made in a longitudinal direction through the corpus uteri or lower segment caesarean section were transverse incision is made in the lower segment.

Historians agree that the term caesarean section is considered to have come from Roman law, entitled (lex regia).This law is alleged to have ordered that a dead or dying pregnant women should have an abdominal delivery to preserve her child for the state. (lex regia) eventually became known as lex caesarica. It is obvious that the technique was known and practised in their time[1].

The first recorded caesarean section on a living woman occurred in 1500, and was performed by a Swiss man, Jacob Nufer, on his wife[2]. In the UK, the first recorded caesarean section on a living woman was performed in Edinburgh by Robert Smith in 1737[3]. The rate of caesarean section has steadily increased from about 5% to more than 20% in the past 20 years due to the reduction in the number of forceps and vaginal breech deliveries, greater awareness of serious foetal distress with use of foetal monitoring during labour and the belief that once a woman has had one caesarean delivery, all subsequent pregnancies must be delivered by caesarean section[4].

Materials and Methods

A retrospective study was carried out on 5403 deliveries undergoing caesarean section both elective and emergency. All cases were admitted to labour room and surgery done at Jamahiriya maternity hospital in Benghazi by SHO, specialist and consultant doctors .The data collected from the files of the statistical department of the hospital from the patients who had caesarean section in the period from January 1998 to the end of December 2000.

Results

The total number of deliveries was 46467. Over the study period, 5403 cases were delivered by caesarean section. The rate of caesarean section at Jamahiriya hospital was 11.6%.

There were 2937 (54.35%) emergency caesarean sections and 2466 (45.64) elective caesarean sections.

The rate of caesarean sections rose from 10.95% in 1998 to 13.05 in 2000 as shown in table I.

The most common indications for the emergency caesarean section were foetal distress (18.36%) and no progress (18.04%). Obstructed labour, placental causes and other indications such as eclampsia, malpresentation, cord prolapse, failed induction, and repeated scar in labour were less common indications for an emergency caesarean section. For elective caesarean section the most common indication was repeated scar (16.93%) as shown in table II.

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Table I. The rate of caesarean section in Jamahiriya hospital in the years 1998, 1999, 2000.

Year	Eme .c/s	%	Elec. c/s	%	Total No. of c/s	Total delivery	%
1998	929	55.29	751	44.78	1680	15338	10.95
1999	913	53.70	787	46.29	1700	15630	10.87
2000	1095	54.12	928	45.87	2023	15499	13.05
Total	2937	54.35	2466	45.64	5403	46467	11.62

Table II. The indications of caesarean section.

Indication for emergency C/S.	NO.	%	Indication for elective C/S.	NO.	%
Foetal distress	992	18.36	Repeated scar(>2 c/s)	915	16.93
No progress	975	18.04	Big foetus	703	13.00
Obst. labour	367	6.79	Placenta previae.	340	6.29
Placenta pre.	295	5.45	Primi breech	173	3.20
Abr. placenta	120	2.22	Previous c/s breech	142	2.62
Other	188	3.40	other	193	3.57
Total	2937	54.4	total	2466	45.6

The rate of caesarean section was highest in the age group 26-30 years (25%) and in para1 (24%) as shown in table III, and the rate was less among the age group above 40 years and in para 4 table III.

Over all wound infection (2.77%), haemorrhage (1.33%) and urinary tract infection (1.24%) were the most common complications while the scar dehiscence (0.46%) bladder injury (0.37%), caesarean hysterectomy (0.24%), wound haematoma (0.22%) and bowel injury (0.05%) were rare complications, as shown in table IV.

Table IV. Frequency of the complications of caesarean section.

Complication	NO.	%
Wound infection	150	2.77
Haemorrhage	72	1.33
Urinary tract infection	67	1.24
Scar dehiscence	25	0.46
Bladder injury	20	0.376
Caesarean hysterectomy	15	0.24
Wound haematoma	12	0.22
Bowel injury	3	0.055

Table III. Rate of caesarean section in relation to the age and parity

Age	Count	%	Parity	Count	%
15-20	470	8.69	Primi	1053	19.48
21-25	1113	20.59	1	1297	24.00
26-30	1351	25.00	2	919	17.00
31-35	1025	18.97	3	734	13.56
36-40	821	15.19	4	617	11.419
>40	623	11.53	5 and More	783	14.5
Total	5403	100%	Total	5403	100%

Discussion

The caesarean section rate at Jamahiriya hospital rose from 10.95 to 13.05% during the period of the study. The rising caesarean section rate is a worldwide phenomenon, more apparent in the developed than the developing countries. In USA, 23 hospitals in southern California had caesarean section rate 33% or greater , five of these had rate of 37-39% [5]. In Canada the caesarean section rate more than doubled from 6 to 13.9% during the 1970s [6]. In Sweden the caesarean section rate has increased from 0.87% (1946-1950) to 11.9% in 1976 [7]. In England and Wales the incidence was 3.1% in 1963 and increased to 7.5% by 1978 [8], the incidence increased to 10% in 1982-1984 [9]. In the underdeveloped countries the caesarean section is low; In Guyana 3% and is comparable to that found on other hospitals in the west Indies [10]

The rising rate also means an increasing number of pregnancies following previous caesarean section. thereby increasing the number of pregnancies at risk of scar rupture.

In our study foetal distress was the most common indication for emergency caesarean section. Foetal distress in labour is an acceptable indication for caesarean section, However identification of the foetus at risk from hypoxia is not always easy.

The diagnosis of hypoxia based on cardiotocography alone has lead to an increase in caesarean section rate. In France, Peter [11] found that foetal distress was the cause of one quarter of caesarean sections in their study.

Ayromlooi and Garfinkel [12] found that foetal blood sampling has helped reducing caesarean section rate. MacDonald [13] however, has shown that electronic foetal monitoring did not influence the number of caesarean section in low risk

pregnancies at the national maternity hospital, Dublin.

In our report repeated scar was the most common indication for elective caesarean section .A high figure 30% was reported by Taylor[14].

Graham's found that 37% of the indications for caesarean section were repeated caesarean.He estimated that if trial of labour had been contemplated for all suitable patients in his series, even with a 50% success rate, it would have reduced the caesarean section incidence from 19-15%[15].

Overall wound infection and maternal haemorrhage were the most common complications. There is a risk of wound infection for women undergoing both emergency and elective caesarean section. Beatie reported as many as one in four women in the untreated groups of randomised, controlled trials of antibiotics at caesarean section developed a wound infection[16]. In our study the rate of wound infection was low and was same for both emergency and elective caesarean section.

Haemorrhage with the need for blood transfusion is one of the more common intra-operative complication at caesarean section. The average blood loss at caesarean section is about 700-1100 c.c. By anticipation the risk factors of haemorrhage and taking the appropriate precaution will minimise blood loss at operation. Uses of different procedures to control haemorrhage will reduce maternal mortality and morbidity[17,18]. In our study 72 cases have had significant blood loss and 15 cases ended by caesarean hysterectomy. Urinary tract infection also is a post-caesarean section problem with the reported rates of bacteruria of 20% postcatheterisation[19]. In our study Foley's catheter was inserted from 8-24 hrs and the incidence of urinary tract infection was 1.24%. Chest infection and endometritis were not recorded during our study. The risk of bladder or uretertic injury at caesarean section is less than 1%. The bladder is most commonly injured during downward dissection before entry to the uterus particularly in a repeat caesarean section[20].There was no ureteric injury in our study but bladder injury occure in 0.376%.It was discovered and repaired at the time of the caesarean section. Bowel injury is rare at caesarean section but may occur particularly during a repeat procedure or if adhesion from previous surgery is present[21], we reported 0.055% cases in our study with bowel injury have had previous scar and adhesion.

Haematoma at the wound and scar dehiscence were rare and no maternal death as complication of caesarean section.

Conclusion

The caesarean section rate in our hospital continues to rise and the rising caesarean section rate is a worldwide phenomenon, more apparent in the developed than the developing countries. Our findings were generally comparable with developed countries and high compared to the developing countries.

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Spontaneous Cure of Infertility

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الملخص

دراسة ملاحظاتية هدفها تعيين معدل عدم الخصوبة الذي خضع إلى العلاج التلقائي بين الأزواج العقيمين ومقارنة ذلك بدراسات أخرى وأيضا تقييم الاختبارات التشخيصية خلال فترة 5 سنوات مضت. 272 حمل حدث بين 1360 زوج عقيم منها 52حمل كان تلقائي , وبدون علاج 19.11 % . السبب الرئيسي لعدم الحمل كان ضعف الاباضة 48.1 % تليه أسباب أنثوية متعددة تمثل 19.2% ، عوامل ذكرية وأنثوية مجتمعة 14.4% . حدث الحمل بطريقة عفوية إما بسبب تصحيح تلقائي لضعف الاباضة أو بسبب تأثير على المدى البعيد لعلاج مسبق. بينت هذه الدراسة إن الاختبارات القياسية لعدم الخصوبة لا يحتمل إن يكون عندها قيمة تنبؤية حقيقية

Abstract

Aims: To determine the incidence of treatment for independent pregnancy among infertile couples. To also evaluate the type of infertility that undergoes spontaneous cure and to compare our findings with other comparable studies, and Finally to assess the value of infertility diagnostic tests. **Design**: Observational prospective study. **Results:** During a five year period, 272 pregnancies occurred among 1360 infertile couples. In 52 couples the pregnancy was treatment-independent. The rate of treatment-independent pregnancies was 19.11%. The most common aetiological factor for infertility was poor ovulation (48.1%) followed by multiple female factors (19.2%), combined with male and female factors (14.4%). **Conclusion:** Spontaneous pregnancy can be expected to occur in patients with poor ovulation either due to the long term effect of prior therapy with ovulation-inducing agents, or due to spontaneous correction of poor ovulation However, in couple with severe reproductive disorders, treatment appeared to be superior to expectant management as the treatment independent pregnancy in this group appeared to be very low. The standard investigation tests for infertility may not have a real prognostic value as 43 couples (86) in the present study were completely investigated prior to occurrence of spontaneous pregnancy.

Introduction

Spontaneous pregnancy occurs frequently in couples who have been diagnosed as infertile but either have received any treatment or have stopped all the treatment.

The proportion of treatment-independent pregnancies ranged from 21 to 62% in studies that included both treated and untreated infertile couples [1,4]. This variability exists, at least partially, because the terminology and definition for pregnancy occurring independently of treatment for infertility have been inconsistent. Some authors have counted only pregnancies that occurred in untreated couples as treatment independent pregnancies[2,3], whereas others have included pregnancies occurring later than some defined period after treatment[1,4]. The second method provides a more complete picture of the proportion of "treatment-independent pregnancies" which refer here to the sum of pregnancies in untreated couples and pregnancies occurring long after treatment in treated couples. In this context, "treatment" means prescribed drugs, surgery or assisted reproductive techniques.

Patients and Methods

From August 1st, 1996 to July 31, 2001, 1700 couples registered at Al-Mokhtar infertility clinic with reported infertility of at least 12 months duration. During this period, 20% of couples left and therefore excluded from this study. After registration of the couples, a detailed history was taken and physical examination performed. The diagnostic evaluation included hormonal assay, hysterosalpingography, a semen analysis and post-coital test.

Laproscopy and chromotubation were performed if there were abnormal findings on the initial pelvic examination or abnormal hysterosalpingography or if pregnancy did not occur within one to two years after registration.

Ovulatory Deficiency: was diagnosed from the menstrual history, hormonal assay and sonographic assessment. **Tubal Defects**: were diagnosed by hysterosalpingography and/or laproscopy. **Seminal Deficiency**: was defined as a sperm density of less than 20 millions per milliliter or sperm motility of less than 40% or abnormal sperm morphology greater than 60% and required at least two semen analysis. A diagnosis of ***cervical factor*** was made if the higher postcoital test score was less than 5 points. Couples with no abnormalities revealed by conventional tests were classified as having unexplained infertility.

All pregnancies were confirmed by pregnancy tests, sonographic examinations, delivery or pathology reports and were classified as occurring in treated or non-treated couples. Treatment-independent refers to those pregnancies occurring spontaneously or following cessation of medical treatment for at least 3 months or 6 months following surgery.

Results

During five-year period, there were 272 pregnancies among 1360 infertile couples with a simple pregnancy rate of 20%. In 220 couples (80.8%), the pregnancy was treatment-related while it was treatment-independent (spontaneous) in 52 couples

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(19.2%). In treatment-independent groups, the women's age ranged from 20 to 41 years with a mean of 29.7 years.

Primary and secondary infertility was equally diagnosed in 52 couples 50%. The duration of infertility ranged from one to thirteen years with a mean of 3.17 years. The a etiology of infertility is summarized in table (1), the commonest single aethiologic factor was poor ovulation and it was detected in 25 women (48.1%), sixteen of them (64%) had a prior therapy with ovulation-inducing agents table (2) and they stopped treatment for at least 3 months before the occurrence of spontaneous pregnancy. The remaining nine women (36%) received no treatment at all prior to conception.

Table (1): Aetiology of infertility among 52 couples

Aetiology	No.	%
Poor ovulation	25	48.1
Multiple female factors	10	19.2
Combined male and female factors	08	14.4
Undetermined	09	17.3
Total	52	100

Multiple female factors were diagnosed in 10 women (19.2%). In addition to poor ovulation associated with polycystic ovarian syndrome (PCOS), other aethiologic factors included galactorrhoea and/or hyperprolactinaemia, uterine factors e.g. septum or fibroid, and unilateral tubal obstruction.

Table (2): Protocols of prior induction of ovulation in poor ovulation group

Ovulation-inducing agents	No.	%
Clomophen citrate (CC)	4	25
CC/HCG	3	18.75
CC/bromocriptine	1	6.25
CC/Dexamethasone	1	6.25
CC/hMG/hCG	4	25
hMG/GRH-a, FSH/hCG, hMG/hCG	1	6.25
hMG/hCG, CC/hMG/hCG	1	6.25
hMG/hCG	1	6.25
Total	16	100

hMG: human menopausal gonadotropins
hCG: human chorionic gonadotropins
GRH-a: Gonodotropin Releasing homogonist
FSH: Follicular stimulating hormone

In nine couples, the etiology of infertility was combined male and female factors e.g. PCOS and oligospermia in 5 couples, accessory male glands infection and poor ovulation in the other 4 couples.

In the remaining nine couples, the cause of infertility was undetermined and seven women were pregnant at the initial visit while one women conceived following hysterosalpingography and another women conceived before completion of the required diagnostic investigations.

Discussion

The incidence of spontaneous or treatment-independent pregnancy in this series was 19.2% and as mentioned earlier, the reported incidence ranged from 21% to 62% [1-4].

Pregnancy can be expected to occur among untreated couples with unexplained infertility[5] but it has also been reported to occur among women whose fallopian tubes appeared to be completely obstructed[6] or whose male partners seemed severely infertile[7]. Treatment-independent pregnancy also occurs after pregnancy following treatment for infertility.

Although treatment-independent pregnancy is common, controlled studies of therapy for infertility are unusual[7].

In our series, spontaneous pregnancy had occurred in 25 women (48.1%) with a diagnosis of poor ovulation and in another 10 women (19.2%) they had in addition to poor ovulation another aetiologies such as galactorrhoea and/or hyperprolactinemia, uterine factor and unilateral tubal block.

In the first group 16 women had treatment for induction of ovulation and they stopped all treatments for at least 3 months before the occurrence of pregnancy. Several authors have reported the occurrence of spontaneous pregnancy following induction of ovulation. Black et al[8] described 21% spontaneous pregnancy rate in 19 women who had previously conceived following hMG/hCG treatment. Gemzell[9] reported 8 spontaneous pregnancies out of 101 women who had previously conceived following human pituitary gonadotropin therapy.

Tymor and Thompson[10] reported 72 women who were treated for induction of ovulation with menotropins, 38 women conceived spontaneously. Zion Ben-Rafael et al had reported treatment-independent pregnancies following human-menopausal gonadotropin-induced pregnancy[11].

These authors have suggested that induction of ovulation and the ensuing pregnancy have a long range therapeutic effect on these women, but Marshall[12] doubts this, in light of the well-known fact that spontaneous pregnancy does occur in anovulatory women. In 9 couples of this series, infertility was due to combined male and female factors, 5 couples had oligospermia and poor ovulation. Nelson and Bunge[13] reported that 20% of males undergoing vasectomy and presumably fertile had sperm counts below 20 million/milliliter. Zukerman et al[14] found that 23% of fertile males had sperm counts below 20 million /milliliter, and they suggested that sperm counts above 10 million/milliliter, should be considered normal. VanZyl et al[15] reported 14 pregnancies in 27 couples (52%) in whom the sperm counts were less than 10 million/milliliter, and a reasonable percentage of pregnancies occurred even with counts below 5 millions / milliliter in couples with a compliant of infertility[16].

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John A. Collins et al reported a spontaneous pregnancy in 44% of couples with poor ovulation[17], and Fadini R. et al[18] described a spontaneous pregnancy rate of 11.1%. The aetiological factors for infertility in this group was 48.1% as a male factor, 41.5% as a female factor and 14.8% diagnosed as having an unexplained infertility. They also found a considerable incidence of pathologies in couples that obtained a spontaneous pregnancy and their findings suggest that common investigation for infertility may not have a real prognostic value.

In a study of treatment-dependent and treatment-independent pregnancies among women with periadenxal adhesions, Tulandi T. et al[19] reported accumulative pregnancy rate at 12 and 24 months follow up (using life-table analysis) showed 32% and 34% in treated infertile women with periadenxal adhesions versus 11% and 16% in the non-treated group. They suggest that although pregnancy might occur in infertile women who have periadenxal adhesions, treatment with salpingolysis is associated with a higher pregnancy rate.

Spontaneous pregnancies have been reported to occur in women with minimal and mild endometriosis, however, the pregnancy rate was higher in treated than non-treated groups[20]. In patients with severe reproductive disorders on waiting list for IVF or ICSI[21], spontaneous pregnancy had occurred in 76 of 1319 women giving a treatment-independent pregnancy rate of 5.4%. 12 months cumulative pregnancy rate for patients on waiting list was 2.4% (95% CI 1.2-3.9%) for tubal infertility, 5.9% (3.7-8.7%) for long standing unexplained infertility and 6.6% (4.5-9.3%) for male infertility. Of 76 controlled patients, 21% of tubal infertility, 8% of unexplained infertility and 17% of male infertility patients achieved a pregnancy in their first IVF or ICSI treatment. The authors confirmed that treatment-independent pregnancy rate in patients with severe reproductive disorders is low. They also concluded that one cycle IVF or ICSI is superior to 12 months of expectant management in patients with severely impaired fertility due to tubal, unexplained or male factors.

Conclusion

The incidence of treatment-independent pregnancy in this series was (19.2%) which is comparable to those reported in the literature. Treatment–independent pregnancy can be expected to occur in anovulatory group of infertile women probably due to either long-term effect of previous therapy with ovulation-inducing agents or spontaneous correction of the anovulatory status. It may also occur, to a lesser extent, in couples with oligospermia and in patients with severe reproductive disorders, the treatment appears to be superior to expectant management.

The standard investigation tests for infertility may not have a real prognostic value as 43 (86%) couples in the present study were completely investigated prior to occurrence of spontaneous pregnancy.

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Maternal Mortality at Jamahiryia Hospital, Benghazi

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الملخص

أهداف الدراسة: معرفة معدل وفيات الأمهات فى مستشفى الجماهيرية على مدى 5 سنوات (1998-2002). **طريقة الدراسة:** دراسة راجعة لملفات المرضى. **النتائج:** تم تسجيل 19 حالة وفاة معطيا بذلك معدل وفاة 28.8 لكل 100000 حالة ولادة حية مع تسجيل أعلى معدل فى سنة 1998 (9 حالات) و أقل معدل فى سنة 2001 (حالة واحدة). **الإستنتاج:** من الأهمية بمكان رفع المستوى التعليمي و الإجتماعى كما وأن تقديم رعاية أفضل للحوامل و إحالة حالات الحمل ذات الإختطار العالي إلى المستشفيات يمكن أن يزيد من خفض معدل الوفيات.

Abstract

Objectives: To determine the maternal mortality rate at Al-Jamahiriya hospital Benghazi in the period of 5 years (1998-2002) **Materials and methods:** A clinic epidemiological retrospective study. Data were retrieved from patient's clinical files. **Results:** 19 deaths were recorded. The calculated maternal mortality rate per 100,000 live births was 28.8. During the study period the highest MMR was 9 (66.8%) in 1998 and the lowest MMR was 1 (7.7%) in 2001. **Conclusion:** The educational and social levels for all women should be improved and better antenatal care with high quality services and referral system of high risk pregnancy to the hospital will further reduce the maternal death and would result in safer motherhood.

Keywords: Maternal mortality, Pregnancy induced hypertension, Caesarean Section.

Introduction

Throughout the world it is estimated that 585,000 women die each year from the causes related to pregnancy and childbirth. Africa has the second highest maternal mortality rate after Asia around 150,000 maternal deaths each year[1].

In Asia and Africa, maternal deaths account between 21% and 40% of all deaths in women during their reproductive age (15-49 years) compared with less than 1% in the United States[2,3] . However, the last three decades have seen a significant decline in MMR in almost all indutrialized and some developing countries, coinciding with the development of new obstetric techniques and improvements in general health status of women[4]. Overall, women in Africa have the highest lifetime risk of maternal death because the high maternal mortality rate is compounded by high fertility. For North Africa, the estimated MMR of 550 per 100,000 live births in conjunction with an average of six births per woman creates an estimated lifetime risk of 1 in 1 and 1750 per 10,000[5]. The earliest recorded MMR for Benghazi during the period 1981-1984 was 21.2 per 100,000 live births[6].

There have been variations, between countries and at different times, in the definition of maternal mortality.(Ninth Revision of the international classification of disease and causes of death (ICD9); World health organization 1977 defines a maternal death as death of a women while pregnant or within 42 days of pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes[7].

Maternal death is subclassified into:

- Direct obstetric deaths resulting from complications of pregnancy, labour or the puerperium, and closely equated with true maternal deaths.
- Indirect obstetric deaths resulting from either a previously existing disease or from a disease developing during pregnancy, not as a result but aggravated by it.

Patients and Methods

The study was carried out at Al-Jamahiriya hospital, Benghazi, which is the main maternity hospital for Benghazi municipality and is the referral hospital for the eastern area of Libya (covering nearly one-third of the Libyan population). More than 95% of deliveries, both normal births and births with complications, take place at the hospital which is equipped with modern obstetric and gynaecological services. The hospital also serves as a teaching institution for undergraduate medical student internees. The average risk in the industrialized countries varies between postgraduates in obstetrics and gynaecology. The prevailing customs prohibit postmortem examination and therefore such evidence is not available.

The study design was a retrospective case series study using medical records and death certificates. Irrespective of the duration of pregnancy, all files

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were reviewed and death certificates were examined to assign an accurate medical cause of death according to the ICD-10 classification. The variables included were maternal age, parity, obstetric history, and gestation period; plus medical condition and diagnosis on admission and causes of death.

Results

Over the 5 year period (1998-2002) there were 65883 live births and 19 maternal deaths. The maternal mortality rate per 100.000 live births was 28.8, ranging from 7.7 in 2001 to 66.8 in 1998 as shown in table I.

Table I. Maternal mortality at Jamahiriya hospital Benghazi 1998-2002.

Year	Live births	Maternal deaths	MMR /100000 live Births
1998	13464	9	66.8
1999	13693	3	21.9
2000	13347	3	22.4
2001	12465	1	7.7
2002	12914	3	23.2
1998-2002	65883	19	28.8

Fourteen (73.6%) women were Libyan, 3 (15.7%) Ghanian and 2 (10.5%) women were Nigerian. All women were Benghazi residents and none of them were educated. Age was varied between 26-40 years and, there were 10 (52.6%) between 26-30 years of age, 4 (21.05%) between 31-36 years of age and 5 (26.31%) between 36-40 years of age. Parity ranged from 1-7, there were 12 (63.15%) with low parity (3 or less deliveries), and 7 (36.8%) have had high parity (more than 3 deliveries).

Nine (47.36%) women have no pre-exiting medical risk, 3 (15.79%) have had PIH, 2 (10.5%) women with D.M, 2(10.5%) women with chronic anaemia, 2 (10.5%) women have had previous scar of caesarean section and only 1 (5.26%) has been treated for DVT. Seventeen (89.4%) women were unbooked, only 2 (10.5%) women were booked with irregular visits.

The gestational age ranged from 28-40 weeks, the average level of Hb ranged from 6.1-11.7 g/dl. Ten (52.6%) women gave birth vaginally while 9 (47.3%) women delivered by emergency caesarean section. On admission 6 (31.5%) women had eclampsia, 6 (31.5%) have had ante partum haemorrhage, 3 (15.78%) of them had abruptio placenta and another 3 (15.78) had placenta preavia. 2 (10.5%) had D.M, 2 (10.5%) women with previous caesarean scar, 2 (10.5%) women in normal labour and 1 (5.26%) severe anaemia. 12 (63.01%) died within 48 hours of deliveries, while 7 (36.8%) within the first week.

There was direct cause of death for 17 (87.47%) and indirect causes for 2 (10.52%). The most common direct obstetrics causes were eclampsia 6 (31.57%), pulmonary embolism 6 (31.57%) and haemorrhage 5 (26.3%) and indirect causes were 1 (5.26%) with severe anaemia and heart failure and 1 (5.26%) uncontrolled D.M as shown in the table II.

Discussion

This study refers to hospital deaths before discharge, directly or indirectly connected with pregnancy, labour or postpartum.

For the period 1998-2002 the MMR 28.8 per 100,000 live births it fluctuated between 7.7 per 100000 live births in 2001 and 66.8 per 100,000 live births in 1998.This rate was higher than the rate at al-Jamahiriya hospital between 1981-1984[6]. Furthermore, in countries of the Eastern Mediaterranean Region, MMR ranged from 0 per 100,000 live births for Cyprus to 11000 live births for republic of Yemen and 1700 per 100,000 live births for Afghanistan[1,2,8]. Therefore, our rate was higher than most industrialized countries and for some developing countries.

The cumulative risk for all women who died was possibly because non of them was educated and all of them were unbooked except two women with irregular visits. Similar to the previous studies in the period of 1981-1984, most deaths (89.47%) at Al-Jamahyiria hospital were due to direct causes. Among the direct causes eclampsia and pulmonary embolism were the most common medical causes of maternal deaths; followed by haemorrhage.

By contrast at present the three leading causes of maternal deaths in USA and U.K[9] are pregnancy induced hypertension, pulmonary embolism and haemorrhage, similar to the causes found in Benghazi. Two indirect causes one of them die due to severe anaemia and heart failure and other by uncontrolled D.M.

Uniform absences of antenatal care and presences of PIH and anaemia among most of the women and late attendance at the hospital by women with serious complications are some of the many circumstances which may ultimately result in death.

In Al-Jamahiryia hospital we believe the main measures which will further lower the maternal mortality will be raising of the educational and social levels for all women, assessment of the risks before and during pregnancy, antenatal care with high quality services at the mother and child health care centres, early referral of high risk pregnancies to the maternity hospital and management of complicated cases by senior staff at the hospital, follow up at pre-pregnancy clinic to assess the fitness for pregnancy and the family planning for use of contraceptives and spacing, all these factors might help to reduce the maternal mortality and result in safer motherhood.

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An Assay for Phospholipase D and the Effect of Pyridoxal-5-Phosphate on the Assay

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الملخص

يعتبر الثرومبوكسان عامل أساسي لتكدس الصفيحات. و هو يتكون من حامض الأراكودينيك الناتج بدوره عن عمل الفوسفوليبيز أ2 على فوسفوليبيدات غشاء الصفيحات. بالأضافة ألى ذلك فإن حامض الأراكيدونيك يمكن اشتقاقه من حامض الفوسفاتيديك. يعتبر البايرودوكسال-5-فوسفات مانع قوى لتكدس الصفيحات و بطريقة غير محددة بعد. تم تطوير مقايسة خاصة بالفوسفوليبيز نوع د و تم تقدير تأثير البايرودوكسال-5-فوسفات على هذه المقايسة محاولين بهذا شرح طبيعة تأثيره المثبط على تكدس الصفيحات.

Abstract

Thromboxane is a basic factor for platelet aggregation. Thromboxane is formed from arachidonic acid which is derived from platelet membrane phospholipids by the action of PLA_2. In addition, arachidonicacid can be derived from phosphatidic acid; a product of PLD action. PLP is known as a potent inhibitor of platelet aggregation, the mechanism of which is not determined. An assay for PLD was developed and the effect of PLP on the assay was examined in an attempt to explain the nature of the inhibitory effect of PLP on platelet function.

Keywords: Platelets, Thromboxane, Aggregation, Arachidonic, pyridoxal phosphate.

Introduction

Phospholipases are enzymes which catalyze the hydrolysis of phospholipids. In general, phospholipases have specificity for the position on the glycerophospholipids backbone rather than for a particular fatty acid. There are five types of phospholipases known (phospholipase A, A_2, B, C and D). phospholipase D (PLD) catalyzes the hydrolysis of the phosphodiester bond between phosphatidic acid and the alcohol moiety of a variety of phospholipases. For example phosphatidylcholine is hydrolyzed by PLD to phosphatidic acid and choline. It has been reported that pyridoxal-5-phosphate (PLP) has an inhibitory effect on the aggregation of blood platelets. This was first reported by Subbarao et al., 1977[1] and then followed by many reporters[2-6]. The mechanism(s) of the inhibitory action of PLP on platelet aggregation has not yet been explained. One possibility is that PLP inhibits platelet phospholipases, thus preventing the formation of arachidonic acid, and therefore inhibiting platelet aggregation. We examined the effect of PLP on phospholipase C and A_2 in previous works[7,8]. Attention in this work was turned to the second product of PLD action; phosphatidic acid which contributes to thromboxane formation (and therefore to platelet activation).
For this, the possibility that thin layer chromatography (TLC) may be used as a semi-quantitative assay of the enzyme activity was examined.

Materials and Methods

Phospholipase D, type V (from cabbage), L-α phosphatidyl choline (L-α Lecithin), type III (from soybean), L-α phosphatidic acid from egg yolk and pyridoxal-5-phosphate were obtained from Sigma Chemical Co. London, England. All other chemicals were of analytical grade.
The assay mixture contained 1.25 ml sodium acetate buffer (pH 5.6), 0.25 ml 1M Calcium Chloride, 1.0 ml phosphatidylcholine (5 mg/ml) and 3.0 ml PLD enzyme solution (5 units/ml). The assay mixture was placed in a stoppered tube and shaken in an incubating shaker at 250 r.p.m for 4 hrs at 30° C. The reaction was stopped by the addition of 0.5 ml glacial acetic acid. Phospholipids were extracted, separated by TLC and identified by iodine. The mixture was shaken after the addition of 4 ml chloroform-methanol solution (2:1,v/v), the lower chloroform layer containing phosphatidic acid was extracted with Pasteur pipette and tubes were placed in warm water bath and evaporated to dryness under nitrogen gas. The resulting residues were re-dissolved in 0.1 ml chloroform: methanol: water solution (70:25:5,v/v). aliquots of 10 µl were spotted onto silica gel TLC plate which has been activated by heating to 100°C for one hour. For the control assay, the above procedure was repeated in the absence of the enzyme. Phosphatidylcholine (5 mg/ml) and phosphatidic acid (5 mg/ml) were also spotted as standards. A zero time

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control was also included. The plates were placed in a chromatographic tank containing chloroform: methanol: water (65:30:5,v/v). the plates were allowed to develop for 90 min, dried and placed in an iodine bath for 10 min for lipid identification.

PLP Stock Solution:

PLP was dissolved in 0.15 N NaOH and kept in the dark or dissolved in 0.15 N NaOH and adjusted to the reaction mixture pH using 1N NaOH. The absorption spectrum of PLP was checked before and after adjusting the solution pH; a characteristic PLP absorption spectrum was obtained in both cases.

Results and Discussion

It may be concluded from the TLC plates that the single spot of the control assay was due to phosphatidylcholine, and the spots of the enzyme assay were due to phosphatidylcholine and phosphatidic acid. A typical TLC plate is shown below (fig.1).

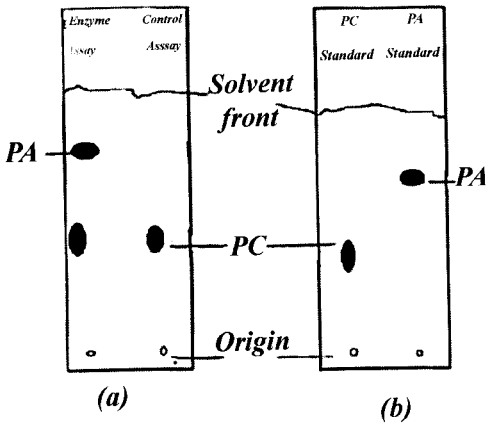

Fig. 1. Typical TLC plates obtained for: a) aliquots of phosphatidylcholine (PC). Control and assay samples. b) aliquots of phosphatidylcholine (PC) and phosphatidic acid (PA) standards.

Samples were run several times on different occasions. From the results shown here, it can be concluded that there was an activity for PLD enzyme and that the assay was satisfactory.

Effect of PLP on the assay

PLP was added to the incubation mixture in the concentration of 1, 2, 3, 5 and 10 mM. Control at zero time and 4 hrs without PLP were included (again, the assay was repeated several times on different occasions). PLP was added to the reaction mixture without and with adjustment of the pH of PLP solution to the reaction mixture pH (5.6). PLP (without pH adjustment) at concentration of 1, 2, and 3 mM had no detectable effect on the activity of PLD enzyme (fig.2). While higher concentration (5 and 10 mM) of PLP were inhibitory; after 5mM PLP addition some phosphatidic acid spots could hardly be detected (fig.2). At 10mM PLP there was full inhibition of PLD enzyme activity concluded from the complete absence of phosphatidic acid spot (fig.2).

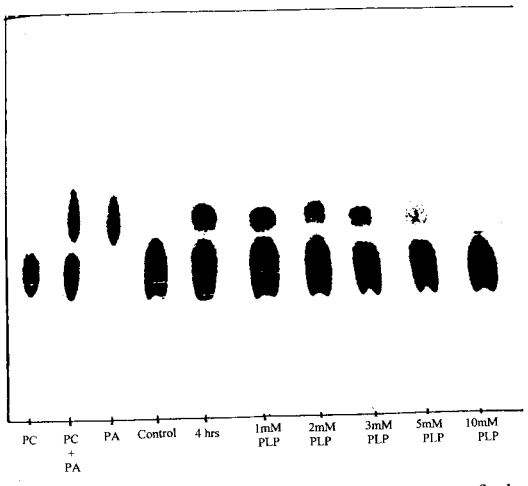

Fig : Typical TLC plate obtained when aliquots of phospholipase D assay mixture were spotted in the absence and the presence of 1, 2, 3, 5 and 10mM PLP. PLP was added without pH adjustment (PC=Phosphatidylcholine, PA=Phosphatidic acid).

When PLP was added to the enzyme assay mixture after being adjusted to the pH of the reaction mixture, no detectable effect on the activity of the PLD enzyme was observed. This was shown by the similarity of the different lanes on the TLC plate in the absence and the presence of PLP (fig.3).

From the above results it can be concluded that a satisfactory assay for PLD enzyme was obtained. Under the present conditions of the enzyme assay, PLP had no detectable effect on the enzyme activity.

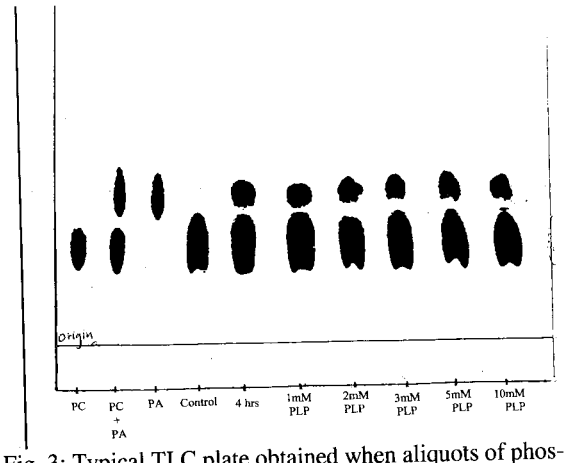

Fig. 3: Typical TLC plate obtained when aliquots of phospholipase D assay mixture were spotted in the presence of 1, 2, 3, 5 and 10mM PLP. PLP solution was adjusted to the reaction mixture PH (5.6) (PC=Phosphatidylcholine, PA= Phosphatidic acid.

The inhibitory effect on the enzyme activity at higher concentration (5, 10 mM) in the first situation, when PLP was added without pH adjustment (fig.2) was only due to pH effect on the reaction mixture; being more acidic in the presence of high concentration of PLP. The results obtained here can be confirmed in a future work by more quantitative methods. For exam-

ple, a radiolabeling assay can be examined, using ^{14}C labelled phosphatidylcholine as the substrate and determining the amount of ^{14}C choline or ^{14}C phosphatidic acid produced.

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Fiberoptic Bronchoscopy in the Diagnosis of Lung Cancer

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الملخص

مقدمة: تم إنشاء وحدة المنظار المرن سنة 1979 أي بعد حوالي 11 سنة فقط من استعمالها بواسطة أكيدا. لوحظ في الفترة الأخيرة انخفاض في النواتج التشخيصية لهذا المنظار. **الهدف**: تحليل الصفات الإشعاعية والهستوباثولوجية والسريرية لمرضى سرطان الرئة. **الطريقة**: دراسة راجعة لكل الذين خضعوا لفحص المنظار الرئوي المرن فة الفترة من 1990-2000 . **النتائج**: العدد إجمالي كان 2368، متوسط العمر 57.8% (34-37). معدل الوفاة 0.04 % ، معدل ناتج الخزعة كان 68.3% مع انخفاض من 76.6% في سنة 1990 إلى 54.2% سنة 2000. **الاستنتاج**: لم يكن ممكنا إرجاع هذا الانخفاض إلى تغيير في كيفية إجراء المنظار أو تغيير العاملين عليه.

Abstract

Background: Our bronchoscopy unit was created in 1979, only eleven years after the introduction of flexible fiberoptic bronchoscopy (FFB) by Ikeda. It has been functioning continuously for more than 20 years, practically, as the only FFB unit in the eastern half of the country. Unfortunately, a decline in the diagnostic yield of bronchoscopic biopsies was noted during the last few years. **Aims:** To analyze clinical, radiological, and histopathologic characteristics of patients with lung cancer bronchoscopied in the last 10 years focusing attention on the diagnostic yield rates of bronchoscopic biopsy. **Methods:** Retrospective analysis of data from all patients who underwent FFB in the period from 1990 to 2000 for the suspicion of bronchogenic carcinoma. **Results:** 2368 patients were analyzed (1687 males and 681 females). The mean age was 57.8 years, (range 34 to 87yrs). The rate of major complications was 1.3% and mortality rate was 0.04%. Bronchial lesion suggestive of neoplastic process was found in 1408 patients (59.5%). The overall yield rate of forceps biopsy was 68.3%. A significant decline in the yield rates was noted from 76.6% in 1990 to 54.2% in 2000. **Conclusions:** The decline in the biopsy yield rates cannot be explained by a change in the procedure or the tools used or a change in the operating personnel. Possible causes are discussed.

Introduction

Bronchoscopy is a useful method for direct visualization of pathological changes in the trachea and bronchi. It was first performed by Killian in 1895.[1] Over the first half of the past century the indications for bronchoscopy have expanded tremendously. Finally, with the introduction of flexible fiberoptic bronchoscopy (FFB) by Ikeda[2] in 1968, the procedure has evolved as the most useful method in the diagnosis of many pulmonary disorders.

The list of indication for FFB is large and still expanding but the diagnosis and staging of lung cancer remains the most important indication. In this study, we report our 10-years experience with 2368 bronchoscopies in patients suspected to have bronchial carcinoma. Indications, clinical and radiological features and complications are discussed. Attention is focused on the diagnostic yield rates of bronchoscopic biopsies.

Patients and Methods

Patients: In a retrospective study we analyzed data from all patients who underwent bronchoscopy in the period from January 1990 to December 2000. All patients to whom the procedure was done with bronchogenic carcinoma as the main suspected diagnosis were selected. Bronchoscopies done for other indications were excluded. Data was obtained from the bronchoscopy unit records, hospital files and records of histopathology department of the medical faculty and the pathology department of Jamahiriya hospital.

The procedure: The procedure was performed transnasally under local anesthesia with an Olympus BF-20D fiberoptic bronchoscope. Pethidine hydrochloride (50 mg IM or IV) was the only premedication given on regular bases. Diazepam was used only for anxious patients and atropine was saved for patients with excessive secretions. Lidocain was used for local anesthesia; 2 to 4 ml of 2% solution in the upper airways, and 8 to 12 ml of 1% solution in the lower airways.

All biopsies of bronchosopically visible lesions were performed using Olympus biopsy forceps. Three to seven samples were obtained from each patient. Specimens were immediately placed in formaline and sent for processing.

The cell type was identified as squamous cell, adenocarcinoma, small cell, or large cell types based on the classification of the WHO[3,4].

Statistical analysis: Proportions and rates were compared by the Chi-square test. Yield rates are calculated according to the formula:

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Number of positive biopsies/total number of biopsies x100.

Results

In the period of 10 years (1990 to 2000), we carried out 2368 bronchoscopies for the diagnosis of bronchogenic carcinoma; 1687 patients (71.2%) were males and 681 (28.8%) were females. The average age (mean ± SD) was 57.8 ± 8.5, (range. 34 to 87).

Indications:

Bronchogenic carcinoma was the main suspected diagnosis in these patients because of the presence of one or more clinical or radiological indications shown in table 1.

Table1: Indication for bronchoscopy in the study group.*

Indication	No. of patients	Percent %
a. Clinical		
Hemoptysis	752	31.8
Unexplained cough	938	39.6
Non-resolving pneumonia	271	11.4
Recurrent laryngeal nerve palsy	98	4.1
SVC obstruction	163	6.9
Shoulder pain ± Horner's syndrome	129	5.4
Search for unknown primary	146	6.2
Abnormal sputum cytology	12	0.5
b. Radiological		
Pulmonary nodule or mass	439	18.5
Irregular pulmonary infiltrate	756	31.9
Consolidation/collapse	342	14.4
Cavity ± fluid level	283	12.0
Hilar enlargement	312	13.2
Widening of superior mediastinum	269	11.4
Diaphragmatic paralysis	136	5.7
Pleural effusion	302	12.8
Normal chest films	93	3.9

*Many patients had more than one.

Complications:

Complications were rare and resulted either from premedications including narcotics or from topical anesthesia or, less commonly, from the procedure itself. Table 2 shows the frequency of minor and major complications. Mild dyspnoea and wheezing due to bronchospasm were the most frequent complications in our patients. Other relatively frequent but transient complications included tachyarrhethmias, hypoxemia and small hemoptysis. Serious complications such as severe respiratory distress, pneumothorax or massive hemoptysis were exceedingly rare.

Table 2: Complications during and immediately after bronchoscopy

Complications	Number	Percent %	Comment
a. MINOR	**271**	**11.4**	
Bronchospasm	29	3.9	Improved with inhaled B_2 agonists.
Hypoxemia	34	1.4	Transient, improved with O2.
Tachyarrhethmias	38	1.6	Sinus tachycardia, PVS
Hemoptysis (<30 ml)	81	3.4	-
Hypoglycemia	17	0.7	Due to unnecessarily prolonged fasting
Epistaxis	5	0.2	Minimal, self – limiting.
Dental damage	3	0.1	-
Urinary retention	1	0.04	Due to atropine
b. MAJOR	**31**	**1.3**	
Severe bronchospasm	11	0.5	8/11 were asthmatic or COPD patients.
Prolonged hypoxemia	1	0.04	Required mechanical ventilation.
Respiratory depression	3	0.1	Due to over sedation.
Hemoptysis (>30 ml)	9	0.4	All treated conservatively.
Pneumothorax	5	0.2	All (except one) associated with TBB.
Seizures	1	0.04	Known epileptic.
Death	1	0.04	Cardiac arrest following local anesthesia.

Only one procedure-related death was recorded in the 10 years period. It resulted from cardiac arrest in a 72 year-old male, immediately following application of local anesthesia to his upper airways. The calculated death rate is 0.04%.

Bronchoscopic findings:

Bronchial lesions suggestive of neoplastic process, either in the form of endobronchial growth or submucosal mural infiltrate, were found in 1408 patients,

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i.e. 59.5% of the total number of bronchoscopies. Table 3 shows the distribution of these findings in the different parts of the tracheobronchial tree. Lesions of both types were seen more commonly in the right side (782 patients or 55.5%) than in the left side (601 patients or 42.7%). The trachea was involved in only 25 patients (1.8%). Upper lobes were involved more frequently; the right more than the left. Together they were involved in 614 patients (43.6%).

Histopathologic findings:

Histopathologic examination of forceps biopsy obtained from the 1408 patients with visible lesions revealed evidence of neoplasms in 961 cases (68.3%). Table 4 shows, the frequency of different histopathologic types. Squamous cell carcinoma was the most common type diagnosed (45.6%), followed by small cell carcinoma (19.6), and Adenocarcinoma (13.2%). Additional 51 cases were diagnosed by other methods; 17 by bronchial washing, 9 by bronchial brushing and 25 by transbronchial biopsy.

Biopsy yield rates:

Table 5 illustrates the effect of the type of the lesion seen at bronchoscopy on the yield rate of forceps biopsy. Positive results, i.e. confirm of the malignant nature of the lesion, was obtained in 83.9% of patients with endobronchial tumors as compared to 46.5% of patients with mural infiltrates. This difference was statistically significant ($P<0.01$).

Table 6 depicts forceps biopsy yield rate calculated separately for each year from 1990 to 2000. A decline in these rates is evident, especially in the last five years.

To study differences in the annual yield rates further we compared the cumulative rates of two 5-year periods; from 1990 to 1994 and 1996 to 2000.

In the first period the calculated yield rate was 77.6% compared to only 55.4% in the second period. The difference was statistically significant ($P<0.05$).

Table 3: Distribution of bronchial lesions in the different parts of the Tracheobronchial tree

Site	Mural infiltrate	Endobronchial growth	Total. N (%)
Trachea	9	16	25 (1.78)
Right side	332	450	782 (55..5)
Main bronchus	56	97	153
Upper lobe	152	207	359
Middle lobe	49	44	93
Lower lobe	75	102	177
Left side	248	353	601 (42.7)
Main bronchus	60	42	102
Upper lobe	106	149	255
Lingula	48	87	135
Lower lobe	34	75	109
TOTAL	589	819	1408 (59..5)

Discussion

Our 10–years experience confirms the safety of FFB. The rate of major complications was 1.3%, which compares favorably with those reported by other authors.[5,6,7,8] Major complications in our study included bronchospasm, hemoptysis and pneumothorax. It should be noted that eight of the eleven patients who developed severe bronchospasm requiring management in ICU were asthmatics. Present consensus, however, favors the pre procedural administration of nebulized bronchodialators in asthmatics.[5,6,9] This complication was potentially preventable.

Table 4: Frequency of the different histopathologic types

HP type	Number	Percentage %
Squamous cell	438	45.6
Small cell	188	19.6
Adenocarcinoma	127	13.2
Large cell	94	9.8
Unclassified & rare tumors	114	11.7
Total	**961**	**68.3 ***

*** % of the total number of biopsies (1408)**

The reported mortality rate due to the procedure is usually low varying in different reports from 0.01 to 0.5.[5,10,11] The mortality rate in our group falls at the lower end of this range and is, therefore, quite acceptable.

Analysis of bronchoscopic findings in our patients revealed two observations, which are, more or less, expected. The first was the predominance of squamous cell carcinoma and, to a lesser extent, small cell carcinoma as the common histopathologic types. This is expected because both types have a tendency towards central location as compared to adenocarcinoma and large cell carcinoma, which explains their relative frequency in patients with bronchoscopically visible tumors.[10,11] The second finding was the common involvement of upper lobe bronchi and the more frequent involvement of the right side compared to the left side, which agrees with many previous reports.[11,12.] The reported average diagnostic yield rate of forceps biopsy in patients with bronchoscopically visible tumors varies in different series from 55% to 85%.[6,10,11,13] Our overall yield rate of 68.3% compares favorably with these reports.

The most important factor in determining the diagnostic yield of forceps biopsy of bronchoscopically visible tumors, in our experience, is the morphology of the lesion. The yield is significantly lower in patients with mural infiltrating lesions than in those with endobronchial exophytic growths.[11,12,14,17]

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Table 5: Effect of the type of Bronchial lesion on biopsy yield.

Type of lesion	No. of patients	No. of +ve biopsies	Yield rate %
Mural infiltrate	589	274	46.5*
Endobronchial growth	819	687	83.9*
All	1408	961	68.3

*** P <0.01**

It was clearly demonstrated that yield rates have declined significantly over the 10-year study period. This progressive decline, which confirms our initial impression, cannot be explained by any change in the technique or accompanying procedures or operating personnel.

The explanation lies, we regrettably believe, in the changes that degraded the histopathology services available to us. Departure of experienced pathologists and lack of basic facilities are among the most important factors.

It would be interesting to see other studies addressing performance of other procedures involving small sample biopsies such as gastroscopy, colonoscopy and cystoscopy in the same period of time. We are certain that results similar to ours would be obtained.

Table 6: Yield rates: 1990-2000.

Year	No. of patients biopsied	No. of +ve histopathology	Yield rate (%)
1990	175	134	76.6
91	158	123	77.8
92	149	119	79.9
93	126	96	76.2
94	172	133	77.3
95	144	88	61.1
96	105	62	59.1
97	94	51	54.3
98	81	45	55.6
99	97	52	53.6
2000	107	58	54.2
Total	1408	961	68.3

Conclusions

1- Flexible fiberoptic bronchoscopy is a very useful procedure for the diagnosis of tracheo bronchial neoplasms and other pulmonarydisorders.

2- It is a quite safe procedure with very low mortality and complication rates.

3- The most important factors in determining biopsy yield rate are location and type of the lesion. The yield is significantly higher with centrally located endobronchial growths.

4- Yield rate in our patients have been declining over the years for reasons thatcould be controlled.

5- However, further studies are required in the future to confirm our findings and possibly, to determine the causes more precisely.

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Identification of a Steroid in Vernix Caseosa with Antibacterial and Antifungal activities

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الملخص

جمعت عشرون عينة عشوائية من مادة الطلاء الدهنى لحديثى الولادة بمستشفى الجماهيرية – بنغازى – ليبيا . أجريت دراسات كيميائية حيوية وجرثومية لفصل الجزء السائل والجزء الزلالى وبيان تأثير هاذين المكونين على بعض الجراثيم مثل إيشريشيا كولاى، كليبسيلاء، والكانديدا فوجد إن هناك نمو لهذه الميكروبات على هذه المواد. أما المكون السائل للطلاء الدهنى فكان مثبط لبعض الكائنات الدقيقة فكانت له خاصية مضادة للبكتيريا والفطريات.

Abstract

Background: Vernix caseosa is thought to have a protectice value for newborns. However, studies of this aspect are limited in number. **Objective:** to determine the effect of Vernix caseosa on the growth of some bacterial and fungal agents. **Materials and Methods:** classical fractionation, saponification and microbiological methods were followed. **Results:** 20 random samples of vernix caseosa were collected form 20 newborns in Jamahyria Hospital, Benghazi – Libya. A Biochemical and microbiological study revealed an isolation of its liquid and protein fraction. Both fractions showed a significant inhibitory effect on E.coli, Klebscilla and Candida Albicans particularly the liquid fraction. **Conclusion:** The liquid fraction (steroidal part) of the vernix is significant inhibitor of some micro-organisms. This steroid found to have antibacterial as well as antifungal activities against E. coli, Klebscilla and Candida.

keywords: vernix caseosa, protein, liquid, steroid, E.coli , Klebscilla, Candida Albican.

Introduction

Vernix caseosa is a white cream like substance produced by the foetal sebaceous glands, which secrete sebum from which vernix is formed[1,2]. Although it plays a significant role in foetal protection in utero, it is usually removed during immediate newborn care[3].

It was recently reported that vernix is used in treating patients with trophic ulcer of lower extremities. Also it was stated that vernix contains long chain fatty acid as well as alcohols[4,5].

Untill now in the available literature, no detailed study has been performed on a possible antibacterial activity of this wax. In addition we don't know which of the fractions has this activity. This stimulated our interest to study a possible antibacterial activity of its lipid and protein fractions.

In addition, isolation and identification of the active molecule in any fraction could be of value.

Materials and Methods

A random sample of 20 vernix collected from 20 newborns immediately after birth at Jamahiriya Hospital, Benghazi-Libya were separately collected in sterile containers.

1. Fractionation of vernix component

A total weight of 2.0g fresh vernix collected from skin of newborn childern, was extracted three times with 10ml petroleum ether. The petroleum ether extracts were evaporated in an oven at 75°C. After dryness, 0.5g of the remaining lipid dissolved in 2 ml 1% sodium dedocyl sulphate and tested for its antibacterial and antifungal activities (A). E.coli, Klebscilla and Candida albicans were used for testing possible activity of that fraction. The remaining part of the vernix (protein) (B) was dried at 100°C then, dissolved in 2 mls of 1% sodium dedocyl sulphate and tested for a possible antimicrobial activity in a way similar to that used for the lipid fraction.

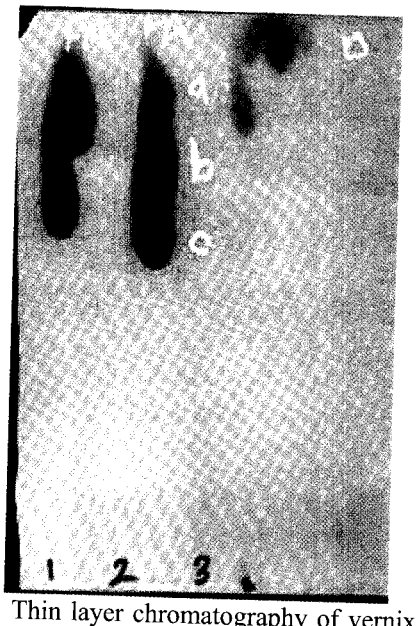

Fig (1): Thin layer chromatography of vernix lipid before and after saponification & its steroid

a- unst. Fas
b- unst. Fas
c- unst. Fas
d- cholester

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2. Saponification of vernix lipids

Two grams of fresh vernix were similarly extracted three times with petroleum ether (10ml each). The extraction was dried in oven at 75°C. Five milliliters of 5% alcoholic sodium hydroxide were added, mixed, and stirred for 30 minutes on water bath 100°C, till complete saponification.

The whole mixture was cooled, acidified with 10ml 10% HCl till neutralisation. Extraction of liberated fatty acids with chloroform (3 times, 5ml each) was done. Thin layer chromatography of this fraction using, ether, petroleum ether, acetone (3:3:1 v/v) in ascending system was performed.

The exctracted lipid fraction was subjected to thin layer chromatography using ether, petroleum ether and acetone (3:3: 1 v/v).

3. Identification of a steroid in vernix lipids

To 0.1ml of chloroformic extract of vernix, 0.5ml of concentrated sulfuric acid was gradually added to form a lower layer. A violet ring between the two layers was observed. To another value of the same extract, one drop ferric chloride (5%) was added, followed by 2 drops of acetic acid anhydride and 1ml of concentrated sulfuric acid. A green color appeared in the lower layer.

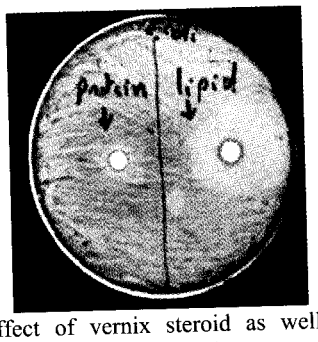

Fig (2): Effect of vernix steroid as well as protein fraction on E. coli (nutrient agar media) .

Results

Thin layer chronatogrophy of vernix lipid before and after saponification is shown in figures 1 and 2 respectively. Figure 3 shows the inhibitory effect of the steroid fraction on the growth of E.coli.

Discussion

Our previous study on human vernix revealed the presence of lipid as a major fraction (62.5%), whereas protein contributed to (36%) and carbohydrate (1.5%)[6] of the vernix.

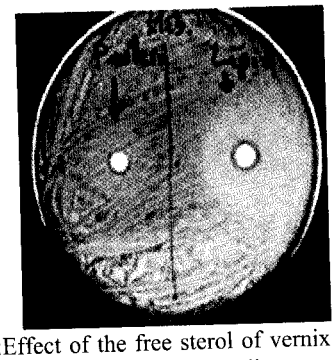

Fig (3):Effect of the free sterol of vernix after liberation of the fatty acid on. E. coli.

Accordingly we can consider this material as an atypical proteolipid. The antiseptic value of vernix previously observed could be explained in our report due to presence of asparagine and glutamine as major amino acid constituents in its protein fraction[7].

Our finding that the lipid fraction of the vernix is a significant inhibitor of some microorganisms stimulated our interest to go deep in this fraction, and finally we could separate and identify a steroidal compound in that vernix. This steroid contains a long chain unsaturated fatty acid esterified with a sterol. Further more antimicrobial activities were found against E-coli, klebsiella and Candida Albicans. Saponification of that active steroid in vernix lipid resulted in liberation of unsaturated fatty acids. Furthermore after losing these fatty acids, the antibacterial (as well as) antifingal properties were retained..This might indicate that a steroid compound similar to fucidic acid [8,9] is one of the components.

Finally, our finding that vernix is active against Candida Albicans is of value specially when we know candida species are found in the vagina [10] and without this vernix foetal attack by that yeast could be fatal. A substantial evidence of our finding is the discovery of an active drug against candida Albicans by polack et al (1983), which inhibits steroid synthesis. So presence of an active steroid in the vernix could show a more or less simillar effect as a foetal protective substance[11].

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Combined Factor V Leiden and Protein S Deficiency (a rare presentation of a rare combination)

(CASE REPORT)

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الملخص

نعرض هنا حالة مريضة ليبية تبلغ من العمر 20 عاما تم فحصها في عيادة مكافحت خثار الدم حيث وجد انها تعاني من خثار عميق في ذراعها الأيسر و تبين لاحقاً أن سبب هذا الخثار غير معتاد الموضع ناتجاً عن عيب جيني في كل من عامل "ليدن" الخامس و بروتن "س".

Abstract

A 20 year old female Libyan patient referred to our anticoagulant clinic with spontaneous left upper extremity deep venous thrombosis. Coagulation studies showed combined genetic defect (Factor V Leiden and protein S deficiency).

Key words: Deep Venous Thrombosis, Factor V Leiden, Protein S.

Introduction

Deep venous thrombosis (DVT) of the upper extremity was first described in late 18th century by Paget and Schroetter and termed as Paget-Schroetter's syndrome[1]. Upper extremity DVT (UEDVT) typically occurs in the axillary or subclavian veins and has been reported in up to 25% of patients with central venous catheters [2]. Other causes include types of external vein compression caused by thoracic outlet obstruction, "effort thrombosis" (found in athletes with hypertrophied muscles), and anatomic anomalies. Spontaneous UEDVT is rare (about 5% of all episodes of DVT) and should raise concern to thrombophilia[acquired (antiphospholipid antibodies) and inherited (antithrombin III deficiency, protein C deficiency, protein S deficiency, Factor V Leiden, Factor II gene mutation G20210A and hyperhomocystinemia)] [3]. We here report a patient who suffered from spontaneous UEDVT associated with combined genetic defect, Factor V Leiden (FVL) and protein S deficiency (PSD).

Case Report

A 20 years old female Libyan patient suffered from left upper extremity pain and swelling. All routine investigations were normal. Doppler ultrasound examination revealed extensive left UEDVT (left internal jugular vein, left subclavian vein and left axillary vein). Magnetic resonance imaging of the thoracic outlet was normal. Screening of thrombophilia (antithrombin III, protein C, protein S, FVL, prothrombin gene mutation and antiphospholipid antibodies) revealed combined genetic defect, PSD {protein S functional activity = 50% - persistent for > 6 months (repeated 2 times)} and heterozygous FVL.

The patient treated initially with heparin and warfarin and then maintained on warfarin.

Discussion

The function of protein C (PC) is to inactivate factor Va (FVa) and factor VIIIa (FVIIIa) (the 'a' denotes the active form). The first step in this process is the activation of thrombomodulin by thrombin, subsequentl, the PC combines with thrombomodulin in order to produce activated PC (APC). APC then combines with protein S (PS) on the surface of a platelet. APC can then degrade FVa and FVIIIa. When one has FVL (Arg506 to Gln), the FVa is resistant to the normal effects of APC, thus the term APC resistance [4] (see diagram 1).

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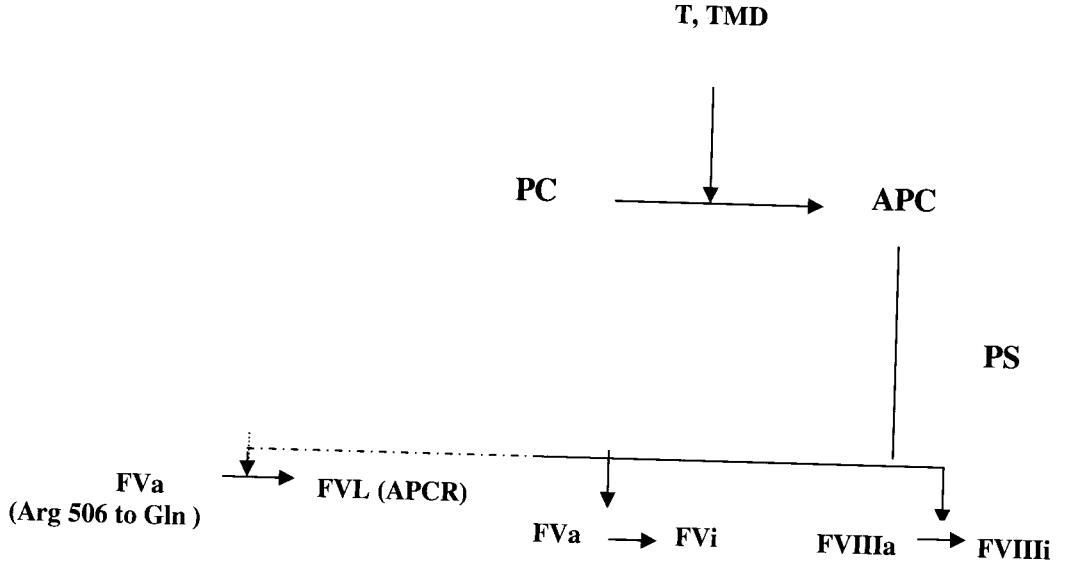

Diagram 1: The protein C-S system

T= thrombin, TMD= thrombomodulin , PC= protein C, APC= activated protein C , PS= protein S, FVIIIa= factor VIII Activated, FVIIIi= factor VIII inactivated, FVa = activated factor V, FVi = inactivated factor V, FVL = factor V Leiden, APCR=activated protein C resistance.

The importance of PS as a natural anticoagulant is manifested by recurrent thrombosis resulting from its deficiency[5]. A carrier of FVL is at increased risk to venous thrombosis[6]. A higher risk for development of thrombosis was found in individuals with combined genetic defect compared with those with a single genetic defect[7]. Our patient is an interesting one in that she had a hypercoagulable state i.e. a combined genetic defect (PSD and heterozygous FVL) that results in spontaneous UEDVT at young age. Carriers of two defects seem to be at a higher risk for thrombosis than their relatives with a single defect. In one review of four studies, approximately 75% of the family members who were carriers of two defects had experienced thrombosis compared with 10 to 30% of the carries of a single defect [8]. Our patient denied any family history of thrombosis and screening of her family for thrombophilia was not possible. Asymptomatic carriers of inherited thrombophilia should take prophylactic anticoagulant at high risk situations (e.g. surgery and pregnancy)[9]. Of concern is that pulmonary embolism is present in an estimated 1/3 of patients with UEDVT[10], so treatment is mandatory. Treatment of non-catheter-associated axillosubclavian DVT suggests that conservative approach (that is, treatment with anticoagulant alone without thrombolytic or surgical therapy) results in a good clinical outcome in most patients. Anatomic abnormalities of the thoracic inlet should, however, be surgically corrected. Catheter- directed thrombolysis, angioplasty, or thrombectomy are unwarranted except in selected cases[11]. The detection of a hypercoagulable state in these patients (like our patient) is important regarding decision of life-long treatment with anticoagulant treatment.

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Transitional Cell Carcinoma in the Lower Ureter in a Solitary kidney

(CASE REPORT)

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الملخص

حالة نادرة لورم سرطاني أحادى الخلية انتقالي ابتدائي من الحالب الأسفل للكلية لرجل في عمر 69 سنة يعانى من تبول دموي. فشلت الموجات فوق الصوتية والأشعة الصبغية للكلي ومنظار المثانة في إظهار السبب الحقيقي لهذه الشكوى.وشخصت الحالة على إنها سرطان الحالب أثناء إجراء فتح استكشافي للمريض.

Abstract

A rare case in primary transitional cell carcinoma of the lower ureter solitary kidney is presented, a 69 years old man was admitted to our hospital with chief complaint of severe macroscopic hematuria and obstructive voiding symptoms in March 2002, KUB x-ray, ultrasonsgraphy, intravenous-pyelogram, nephrostogram and cystoscopy failed to reveal the exact cause of hydrouretronephrosis which was in fact discovered during operation to be urothelial tumor.The patient 9 months after the conservative operation is apparently free of the ureteral tumor.

Introduction

Carcinoma of the renal pelvis and ureter are rare,[1, 3, 4, 9, 11] accounting for only 4% of all urothelial cancer. The ratio of bladder to renal pelvis and ureteral carcinomas is approximately 51:3:1, and the majority of the uretral tumors were in the distal part and approximately 50% of the patients had synchronous or asynchronous urothelial tumors, and male to female ratio is 2-4:1 and twice as common in whites as in black[10, 11].

The peak incidence in white men is 10 cases per 100,000 per year. The mean age of occurrence is 65 years [3, 11].

The history of cigarette smoking is noted in 77% of cases[11]. Supporting the rarity of this lesion herin we present the first case in urology center in Benghazi with a capacity of 2000 urological cases per year in the last 12 years.

Case Report

69 years male Libyan patient presented to our urology O.P.D. with severe total frank hematuria and lower urinary symptoms. Patient gave history of Lt. nephrectomy after a gun shot injury in 1979, and living in an area of endemic schistosomiasis abroad for 20 years. History of non-smoking for the last 20 years.

O/E: patient was pale, a febrile, dyspnic, tachycardia, B.P 100/70.

By investigation patient was azotemic creatinine 2.8 with normal electrolytes, Hb. 8.7 and urine RBC plenty, culture no growth, no bilharzial ova and negative for acid fast bacilli. Tuberculin test was done which was negative. Chest x-ray free. USS revealed sever hydrouretronephrosis. I.V.P. was done which show faint excretion with severe hydrouretronephrosis and the dye stopped at the lower border of the Rt. Sacroiliac joint, both USS and IVP (figure1) couldn't give exact cause of the obstruction. So went to cystoscopy and we couldn't find cause of hematuria, obstruction in the lower urinary tract nor signs of bilharzial infestation and no biopsy was taken from the bladder at that time, we put D.J stent with little resistance about 4 cm from ureteric orifice to improve renal function and overcome the obstruction, after 1 month patient renal function improved from 2.8 to 1.6 and no more frank hematuria and Hb raised to 9.6. DJ stint removed and so we planned him for Rt. Percutaneouse nephrostomy, nephrostogram (figure2) done which also failed to prove the natural cause of the obstruction.

In June 2002 the decision of exploration of the lower ureter and the possibility of lower ureteric stricture as the most likely cause of obstruction was our first impression.

Intra-operative we found fleshy fullness of the lower ureter about 4 cm in length no adhesion around the ureter, the adventia was free. So the decision of the excision with a safety margin of 2 cm above the lesion was taken down to the entrance to the urinary bladder, on opening of the excised part of the ureter we found papillary growth filling the lumen of the ureter and assessment of the regional lymphnodes done which were not enlarged, re-implantation of the ureter without submucosal tunnel was performed. Post – operative period passed smoothly, nephrostomy tube removed and histopathology revealed transitional cell carcinoma grade 2 with no evidence of muscular infiltration.

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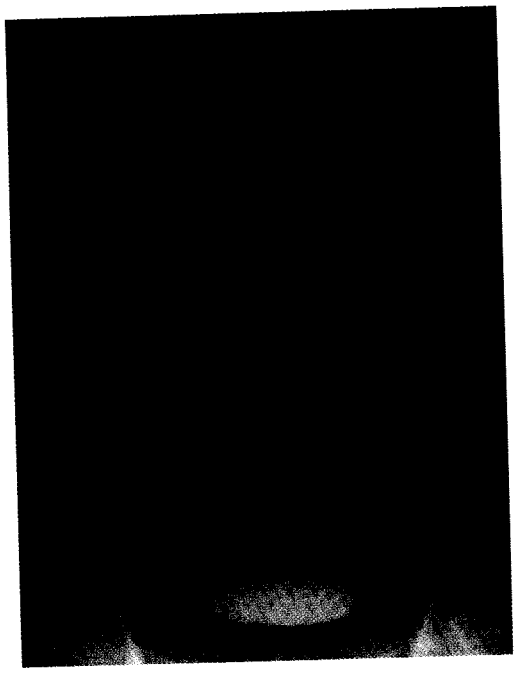

Fig.1: I.V.U. study revealed hold- up of contrast media at the terminal portion of right ureter.

Patient advised to be followed after 2 months to re-check the bladder and 4 random biopsy was taken for the possibility of multicentricity of urethilial wall, which came as chronic non-specific inflammation.
After 9 months the patient came and followed up by testing USS, IVP and cytology which resulted in free of recurrence in all.

Discussion

The most common presenting symptom or sign of upper tract urothelial tumor is gross or microscopic hematuria, flank pain[1, 3, 4, 11]occurring in 75%, 30% respectively our patient presented with hematuria, flank pain, prostatism and azotemia.

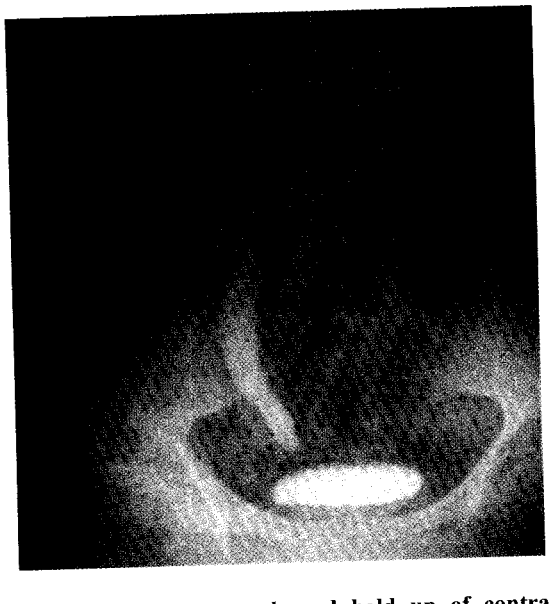

Fig. 2: Nephrostogram showed hold up of contrast approx. 5 cm away from U.V.Junction with evident proximal hydrouretronephrosis.

Upper tract urothelial tumors usually diagnosed as radiolucent filling defects on excretory or retrograde urography, tumor cause obstruction or non visualization of the collecting system in 10-30% as in our patient [1, 3, 4, 7, 11].
Johnson and Babaian 1979 reported that TCC rarely develops subsequently in upper urinary tract above the level of resection of ureteral tumor, so that what we have done in our case especially that he has a solitary kidney. Even some authors reports effectiveness of tranureterial fulguration and resection of the tumor and follow up endoscopy.
As the tumors behave more invasive (anaplastic), the visualization become.

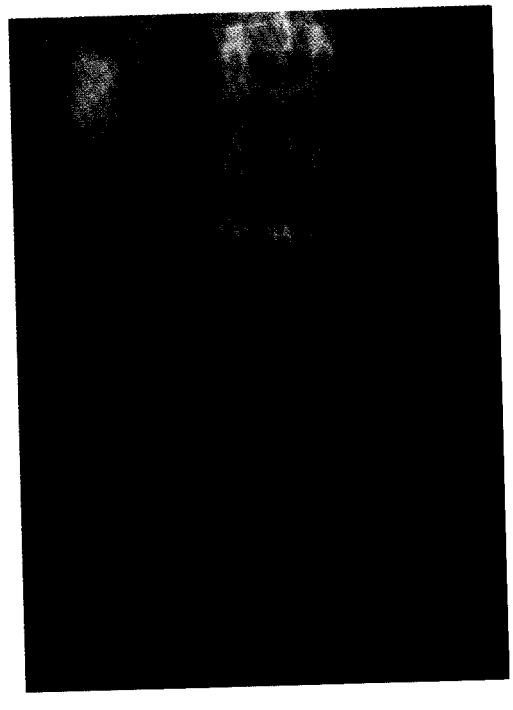

Fig. 3: Post op. findings showed good drainage of contrast from kidney to bladder with no depicted dilation of the ureter.

Conclusion

Since prognosis for patient with low stage tumors was not enhanced by an aggressive operation a more conservative approach is indicated, and the depth of tumor invasion is the most accurate indicator for over – all outcome[1, 4, 8, 11].

Pagano–F in 1984 advised modified uretroneocystostomy avoiding curvature of the ureter for upper urinary tract endoscopic control [5].

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مجلـــة

قـاريونـس الطبيـــة

المجلة الرسمية للكليات الطبية-جامعة قاريونس

ص . ب 5718 بنغازى

الجماهيرية العربية الليبية الشعبية الاشتراكية العظمى

مجلة قاريونس الطبية تصدر مؤقتاً بشكل نصف سنوي وتتناول العلوم الطبية .
مجلد يحوى عددين احدهما فى يناير والآخر فى يوليو

السعر	العملة المحلية	العملة الاجنبية مع رسوم البريد
اشتراك سنوى	16 دينار ليبى	12 دولار
نسخة واحدة	8 دينار ليبى	6 دولار
25 مستخلص من البحث	20 دينار ليبى	15 دولار

تنبيـــه :

- لا تمثل المقالات التى تنشر فى هذه المجلة وجهة نظر الكلية ولا هيئة التحرير ويعتبر الكاتب وحده المسئول عما فيها من آراء وعن صحة ماجاء فى المقالات.
- ينصح الراغبين فى نشر إنتاجهم بقراءة الارشادات المطبوعة للمؤلفين والتقيد بها.

مجلة قاريونس الطبية

الجماهيرية العربية الليبية الشعبية الاشتراكية العظمى