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Medical Research : (II)
Conceptualizing Epidemiologic Research Methods

B. S. Gupta

(Received 24th July 1994)

SUMMARY

Epidemiologic studies are quite popular and widely used to evaluate associations of disease – risk factors, and have made significant contributions in our understanding of disease, or conditions of interest. There are a number of specific study design options that can be employed. A clear and working knowledge of these methods may be helpful to those who plan and conduct research.

Two broad design strategies have been recognized:

Observational and intervention (Experimental). The major difference between the two lies in the role played by the investigator. In observational studies, the investigator simply observes the natural course of events or occurrence of disease in people, who are themselves separated into groups on the basis of some experience or exposure (eg. smokers versus non – smokers or married versus single). In intervention studies, the investigator allocates the exposure group and non – exposure groups and then follows the subjects for the subsequent development of disease. A brief overview of study designs used in observational studies is presented in this paper.

1. Cross – Sectional Study also known as prevalence study. In this study design individuals are concurrently classified as diseased or diseasefree, and exposed or non – exposed, at a single point in time. Prevalence rates are compared between those exposed, and those not exposed to the suspected risk factors (3,5). For example, it has been observed in Cross – Sectional Studies that individuals with cancer have significantly lower levels of serum beta carotene, a vitamin A precursor, than healthy individuals of the same age and set. However, it is not possible to determine from such a design whether the observed low beta carotene levels preceded the development of cancer, which might suggest a possible etiologic role, or whether the low beta carotene levels were in fact a result of disease itself due to dietary changes or the general debilitating effects of cancer (2). Thus crosssectional surveys, while easy and rapid to accomplish, do not establish the temporal (time) sequence of events necessary for drawing casual inferences. However,

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for factors that remain unaltered over time such as sex, race, or blood groups, the cross – sectional study can provide evidence of a valid statistical association, although such instances are rare.

2. Case Control Study (Syn: Retrospective Study, Case Comparison Study). A study that starts with the identification of persons with the disease (or other outcome variable) of interest, and a suitable control (comparison, reference) group of persons without the disease. The relationship of an attribute to the disease is examined by comparing the diseased and non diseased with regard to how frequently the attribute is present or if quantitative, the level of attribute, in each of the groups. Estimation of disease risk associated with exposure is done by Odds ratio, which is typically used to assess the strength of the association between exposure to a suspected cause and disease (3, 4, 6).

A classifed case control study was done by Vassey and Doll (1969) to study the association between thromboembolic disease and use of oral contraceptives. They selected 84 women who had been admitted to hospital with venous thrombosis or pulmonary embolism without medical cause, and another 168 women who had been admitted to the same hospital with other diseases and who were matched for age, marital status and parity. Both groups of women were interviewed regarding use of oral contraceptives. It was found that 50% of those with thromboembolic disease had been using oral contraceptives compared with 14% controls (Table 1). The estimated relative risk (Odds ratio) was 6, indicating that oral contraceptive users were 6 times as likely as non – users to develop thromboembolic disease (9).

3. Cohort Study (Syn: Prospective, Follow Up, Longitudinal, Incidence Study).

The term cohort is defined as a group of individuals sharing a common characteristic or experience (eg. age, occupation, exposure, pregnancy), Thus persons born within a particular period form a 'birth cohort'. Persons exposed to a common drug, vaccine or infection within a defined period constitute an 'exposure cohort,. Persons married on the same day or within a defined period form a' marriage cohort, and so on (4, 5, 7). An essential feature of the method is to follow up healthy cohorts (Study and Comparison) for a sufficient time for the development of disease. The study consists of identification of groups of individuals with and without the characteristic (eg. elevated serum cholesterol) or exposure (eg. smokers and non – smokers) or groups with a gradation or degree of exposure (eg. radiations, smoking). One is known as the study group and another comparison group which are called cohorts.

The groups are then followed over time to determine how frequently cases develop among them. At the end of the follow up period, the indidence rates of disease are calculated in both groups.

A typical example of cohort study is the Framingham heart study (1, 6) which became a prototype of similar studies in other countries. The town of Framingham (Massachussets) had a population of 28,000 in 1948 . The study was planned for 20 years in view of heart disease. A sample of 5209 persons in the age group of 30 – 59 years participated in the study. Information was obtained with respect to serum cholesterol blood

Table 1 : A case control study on the safety of oral contraceptives

Cases/ Venous	Numbers	Percentage who used oral contraceptives
Thrombosis & Pulmonary embolism	84	50
Controls	168	14

pressure, weight, and C. smoking. The study population was followed up and was examined every 2 years for 20 years to detect development of coronary heart disease C.H.D.) With increasing serum cholesterol levels in the 45 – 49 age groups. C. smoking was more strongly associated with sudden death from C.H.D. than with less fatal forms of the disease. Risk factors have been found to include male sex, advancing age, high serum lipid concentrations, high blood pressure, c. smoking, diabetes mellitus, obesity, low vital capacity, and certain E.C.G. abnormalities.

4. Historical Cohort Study (Syn: Historical prospective study, non – concurrent prospective study). A cohort study conducted by reconstructing data about persons at a time or times in the past. This method uses existing records about the health or other relevant aspects of population as it was at the same time in the past, and determines the current or subsequent status of members of this population with respect to the condition of interest (4,5). Seltser and Sartwell (1965) have applied this approach to study mortality of groups of physicians in relation to their possible exposure to radiation (8). Three specialty groups were selected: radiologists, internists and ophthalmologists and otolaryn – gologists to provide a gradient of occupationally related exposure to radiation. Mortality was analysed for two – time periods: 1935 to 1944 and 1955 to 1958. Radiologists had the highest death rates, the ophthalmologist and otolaryngologist the lowest.

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TIMING OF CASE – CONTROL, PROSPECTIVE COHORT AND HISTORICAL COHORT STUDIES IN RELATION TO EXPOSURE AND OUTCOME:

Case – Control Study

Exposure Disease

? ..... 0 ..... Investigator at the beginning

? ..... 0 ..... of study

Prospective – Cohort Study

Exposure Disease

0 – Investigator – ?

O – at the beginning – ?

of study

Historical cohort study

Exposure Disease

0 – ? – – – – – – – – – – – – – – – – – – Investigator

O – ? – – – – – – – – – – – – – – – – – – at the beginning

of study

0 = Present

O = Absent

? = To be determined

= Investigator at the beginning of study.

Basis on which groups are selected at the beginning of study.

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Detection of Salmonella Typhi Antigen in Urine Using Slide Coagglutination Test for the Diagnosis of Typhoid Fever

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(Received on 25th Aug. 92)

SUMMARY

Typhoid fever almost completely disappeared in Western countries, but is one of the major causes of illness in tropical countries like India and certain parts of Africa. Diagnosis by culture, though specific causes delay and difficulties in isolation due to various reasons. The serology though easier, is underserved considering its fallacies and shortcomings with problem of specificity and sensitivity. For early diagnosis of typhoid fever, coagglutination test by Kronvall's method was performed using ruine samples and the results compared with routine procedures like culture and serology.

Three hundred in – patients clinically suspected to be typhoid fever were chosen for the present study. Ninety three cases out of 300 were positive for urine coagglutination test. A control group of 150 healthy medical students showed negative coagglutination.

الملخص

مازالت حمى التايفود إحدى أهم أسباب العلل في المناطق المدارية مثل الهند، غير أنها تكاد تختفي في كثير من البلدان المتقدمة. ورغم أن تشخيص هذا المرض بواسطة الاستنبات (عزل الجرثومة)، والطرق المصلية محدد ودقيق، إلا أن هذه الطرق تحتاج لوقت ليس بالقصير، فضلاً عن صعوبة عزل الجراثيم من العينات بواسطة الاستنبات وذلك لعدة أسباب.

ولكي نتمكن من التشخيص المبكر لحمى التايفود، قمنا بإجراء اختبار مصاحب التراص متبعين في ذلك طريقة كرونفال على عينات البول التي أخذت من 300 مريض مشتبه بحمى التايفود و150 عينه من طلبة أصِّحاء في كلية الطب (استخدمت لمجموعة ضابطه) وقارنا نتائجه بنتائج الطرق الروتينية المستخدمة في المختبرات الطبية كالإستنبات والطرق المصلية.

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INTRODUCTION:

Enteric fever which includes typhoid fever (caused by **Salmonella typhi**) and paratyphoid fever (by **Salmonella paratyphi A,B,C** and **S. sendai**) still remains a major cause of illnesss in tropical countries like India and certain parts of Africa. It has been almost eliminated from developed countries because of better sewage and water treatment facilities. The number of cases occurring yearly was estimated at almost 7 million in Asia, 4 million in Africa and half million in Latin America. Almost 500 cases were diagnosed each year in United States and over half of these were in recently arrived travellers who contracted the infection abroad (7). In India and certain parts of Africa mainly typhoid is present. Paratyphoid A occurs in Eastern Europe, the U.S.A., the Far East and also India. Paratyphoid B is common in Europe and is responsible for 20% of cases in North America. Paratyphoid C is widespread in Guyana and is also found in Eastern Europe (13). The spread of enteric fever is usually by carriers, often food handlers through the contamination of food, milk or water. Infected shell fish are occasionally responsible for an outbreak. In carriers, the bacilli may live in the gall bladder for months or years after clinical recovery and pass intermittently in stools and less commonly in urine. **Salmonella typhi** and **S.** paratyphi B antigens are consistently present in the blood and excreted in the urine during acute stage of illness, but usually ceases in the first 2 months (6). When excretion continues into the third and later months, some abnormality of the urinary tract should be suspected. Sometimes the kidneys are sound and the lesion appears to be in the lower urinary tract. Schistosomiasis, for example, common in Egypt, may provide focus in the bladder wall where certain organisms can find a lodgement (6 , 11). In one investigation, urinary carriers in Egypt formed upto 5% of the special population studies (2).

The diagnosis of these clinical conditions by culture takes time and is very often not successful due to various causes. The serology by widal test, though easier, is undeserved considering its fallacies and shortcomings with problem of specificity and sensitivity (1). So there is a necessity to search for a new diagnostic test for these clinical conditions. In this study we used slide coagglutination method in urine specimens collected from the suspected cases of enteric fever for its diagnosis.

The coagglutination (CoA) method was first introduced by Kronvall (8) for serological typing of Pneumococci by means of specific antibody absorbed to Staphylococcus protein – A. This however was based on the principle that Staphylococci rich protein – A on their outer surface bind IgG non – specifically through the FC region leaving specific Fab sites free. The subsequent reaction of Fab with homologous (test) antigen is visualized by clumping of the Staphylococci. The CoA nowadays is also intended to the identification of **Neisseria gonorrhoeae,** serogrouping of **Streptococcus pyogenes,** detection of Meningococcal, Pneumococcal, Cryptococcal and **Haemophilus influenzae** antigens in CSF (4).

MATERIALS AND METHODS:

Urine specimens were collected from three hundred patients admitted to King George Hospital, Visakhapatnam (India), with clinical history of typhoid fever with the following signs and symptoms were chosen for this study. The onset of fever was insidious with temperature rise in stepladder pattern with increasing headache, malaise, drowsiness and aching in the limbs with or without spleenomegaly. The pulse was often slow with bradycardia. The tongue was dry and coated. The enteric fever was confirmed with blood cultures and widal tests which were used to evaluate the CoA method. The isolated organism was also identified using the conventional methods (3).

One hundred and fifty healthy medical students were chosen for study as control group.

Slide cogglutination test was carried out to detect **S. Typhi** antigen in the obove mentioned groups using urine as specimen.

Preparation of Stabilized Protein – A Rich Staphylococci:

The Cowan 1 protein – A rich Staphylococcus strain was grown confluently on Muller – Hinton agar for 18 hours at 37oC. The growth was suspended in 5 ml of Phosphate Buffered Saline (PBS pH7.2). The suspention was centrifuged at 3000 rpm for 5 minutes and the supernatent discarded. The precipitate was washed three times using PBS and finally 10 per cent V/V of the suspention was heated at 80oC for one hour with constant stirring. It was again centrifuged and washed three times in PBS and stored as a 10 percent V/V stabilized suspension in PBS at 5oC after adjusting the concentration of the bacterial suspension to Brown's opacity tube No.4 until coupled to the antiserum (8).

Coupling of Antibody to Staphylococcus:

The method of kronvall (8) was used to coat the Staphylococcal cells with IgG. The monovalent anti – d **S.typhi** serum was used to couple the cells. One ml of the 10 percent Staphylococcus (Cowan strain 1) preparation was mixed with 0.1 ml undiluted monovalent S. typhi anti – d serum and also normal rabbit serum which was used as a control. The mixtures were left for 3 hours and gently agitated at half hourly intervals. Each lot was used without further washing. Before use. 1 ml of undiluted suspension was diluted with 9 ml of PBS. The final suspension were called as CoA – MVS (Coagglutination Monovalent Serum) and CoA – NRS (Coagglutination Normal Rabbit Serum) respectively.

Test Procedure:

VDRL slides were used to carry out the test. After centrifugation of urine (3000 rpm for 2 minutes), a drop of supernatent was placed in the ring. To each test sample, one drop of final suspension of Staphylococcus – antibody coupled reagent was added and mixed with an applicator and the slide was rotated continuounsly by hand and the readings (Positive or Negative for agglutination) were taken after 30 seconds and before 2 minutes. Positive and negative controls were included in the test. CoA – NRS and stabilized Staphylococcus were used as negative controls.

RESULTS:

Of the 300 patients of suspected typhoid fever, 93 (31%) gave positive results for urine CoA, 58 (19.3%) for culture and 82 (27.3%) for significant widal test (Table I and II).

In control group, both urine CoA and widal tests showed negative results in all 150 healthy medical students.

DISCUSSION:

It is observed from the present study that urine CoA for the detection of antigens of **S. typhi** was positvie in 31 percent of cases compared to culture positive in 19.3 percent and widal positive in 27.3 percent (Table I).

Even though culture was positive in 19.3 percent of cases, it has certain drawbacks. Conventional culture techniques were influenced by factors like stage of disease, administration of antibiotics and techniques like repeated subcultures., The serological "widal" test was positive in 27.3 percent cases, in face of the complicating factors in a widal test, it might be seen that a clearcut diagnostic result was too much to expect from the performance of one widal test. It must be admitted that the test was not a diagnostic one. In an area where the enteric fevers were uncommon, a titre of 1/40 for either H or O or both in an unvaccinated febrile patient should suggest the possibility of enteric infection. Titres over that level have increasing diagnostic significance. In areas where the enteric fevers were common, antibodies due to past infection will be common in population, and it was essential to know the average level of antibodies in normal healthy population in that area (9). In a febrile patient, in such an area, a high 'O' titre was of more significance than 'H' titre and it may be necessary to perform a second test before a valid inference can be drawn from the agglutination titres. In a study in South Africa in 1981 , a titre of 1/200 for O and H antibodies was regarded as strong presumptive evidence of typhoid fever in patients with clinical symptoms,

but a fourfold rise of titre was preferred (12). In vaccinated patient, it may be possible even after a second test to make any reliable deduction. The diagnostic value of the widal test in any give case varies considerably with the knowledge and experience of the interpreter (9).

Even though there is no statistical significance (P value > 0.10) between the results of urine CoA and widal tests (Table II) in the present study, still urine CoA is preferred to widal test because urine CoA test is more convenient, rapid, easier to perform and less difficult to interpret the results than the widal test. Also less expensive and where cost counts for any diagnostic test in a third world country. The test is more specific and more number of cases can be tested at a time with less number of staff.

Similar and more elaborate studies conducted by Rockhill (10) yielded 97 percent positive by urine CoA and culture was positive in 74 percent. Their study included only confirmed typical cases of enteric fever.

The results of the present study were in accordance with the findings of Dhanalakshmi et al (5).

Coagglutination techniques are becoming inceasingly used because they have been shown to be sensitive and specific for identifying many important pathogens with promising results.

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Table 1 : Culture, Widal and Urine CoA positivity in 300 suspected cases of Typhoid fever.

Total Number of Suspected Enteric (Typhoid) Fever Cases	Significant Widal Test (H & O above 100)	Culture Positive	Urine CoA Positive
300	82 (27.3%)	58(19.3%)	93 (31%)

Table II : Evaluation of Urine Coagglutination and Widal Tests

Total No. of suspected enteric (Typhoid) Fever Cases	Significant Widal Test		Urine CoA Positive		X^2	P Value	Remarks
	No	%	No	%			
300	82	27.3	93	31	0.9761	>0.10	Not significant

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Prevalence of Antibodies to Texoplasma Gondii in Pregnant Women and in Different Age Groups in Benghazi

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(Received on 11.08. 1993)

SUMMARY

The prevalence of antibodies to Toxoplasma gondii in pregnant women and in women of childbearing age in Benghazi is 50.1%. The prevalence of antibodies in children is low (10%), and in school girls aged 11 – 20 years is 51% .
Girls may become infected when they reach their late teens. Direct contact with cats did not seem to play a major role in the transmission of the infection and indirect transmission of the infection seems more likely. Contact with contaminated raw meat may be an important way of transmission of the infection in the area.

INTRODUCTION:

Toxoplasma gondii is an obligate intracellular protozoan that causes important diseases in man and domestic animals. Cats are the definitive host and shed millions of oocysts in their faeces each day (8). After sporulation, the oocysts remain infectious in moist soil for longer than one year (5).

Although Toxoplasma infection is found in a large portion of the world's human population, only a relatively few people have toxoplasmosis. Toxoplasma infection may be acute or chronic, symptomatic or asymptomatic. Acute infection is usually asymptomatic in older children and adults: if any signs and symptoms are present, they are commonly of short duration and are self – limited. In most cases, the tissue cyst form of the organism persists but the person has no clinical manifestations (chronic or latent Toxoplasma infection). In a few cases, however, Toxoplasma is the proven cause of persistent or recrudescent clinical manifestations (chronic toxoplasmosis); choridoretinitis (ocular toxoplasmosis) is an example of the chronic form of the disease. Acute infection poses the greatest hazard to the immunodeficient patient and to the infant in utero. In the immunodeficient patient, the infection may reactivate and produce severe and life – threatening disease, such as encephalitis.

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myocarditis, pneumonitis, or a combination of these clinical manifestations. The infant infected in utero – whether asymptomatic or symptomatic at birth – may develop serious untoward sequelae, such as impaired vision, neurologic disorders, and sensorineural hearing loss. Thus congenital Toxoplasma infection may lead to congenital toxoplasosis. The cost to society of caring for patients with congenital toxoplasomsis is enormous.

Libya is a North African country and toxoplasma gondii was first isolated from a North African rodent; Ctenodactylus gondii (8). While there is no doubt that the disease is there, reliable records of proven cases are not available. Our personal contact with some ophthalmologists and paediatricians, working in the city of Benghazi, revealed that there are few cases of toxoplasma and congenital toxoplasmosis with hepatosplenomegaly and skin rash as well as asymptomatic children with intracranial calcification. The preliminary results of an unpublished work on animal toxoplasmosis in Libya show that 13.7% of sheep, 1.8% of goats, 1.8% of camels, and 4.9% of horses are seropositive (Gosbi, A. personal communication). Surveys done in other countries with similar climatalogical, ecological, and social backgrounds show that the prevalence of antibodies to toxoplsama gondii in pregnant women varies between 37.4% and 58.2% (1 ,2). Dar et al. screened 41 women with a history of recurrent abortions for toxoplasma infection in benghazi and showed 62.3% positivity by IFA test(7).

Although the sample size is small and the study group is well defined in this study, the result cannot be ignored as it sheds some light on the problem and is consistent with results in other similar countries. It was felt that it is of importance to screen a larger sample, randomly selected, of pregnant women for antibodies to **T. gondii** to assess the seroprevalence of **Toxoplasma gondii** in pregnant women and other females at different age groups and to determine the age at which girls become infected.

SUBJECTS AND METHODS:

Pregnant women attending antenatal clinics were screened. The main antenatal clinics in the City (Benghazi) were used as they are fairly distributed and drain patients from various socioeconomic groups. Antenatal wards of the "Jamahiriya" Hospital (the only hospital in the city with antenatal wards) were also used. All women attending these antenatal clinics were screened, and no preference was made between attendants. Pregnant women population provided cases for 21 – 30 years and above 30 years age groups. No non pregnant women above 20 years of age were screened. Girls from schools provided the 11 – 20 year age group population. Children attending paediatric clinics, general paediatrics, cardiology and nephrology clinics, provided 0 – 10 year age group population. Infectious disease, neurology and clinics for mentally retarded children were excluded as they could act as a potential gathering of children with known or unknown toxoplasmosis. Again, samples were taken from all girls attending clinics and children admitted to paediatrics wards. Infectious disease ward was excluded.

A brief questionnaire covering subjects particulars' name, age, nationality, as well as possession of cats. was made.

5 – 10 ml venous blood samples were taken from pregnant women, and separated serum samples were tranported and stored frozen till tested. Filter paper samples were taken from children and school girls using Autolet (R) finger prick. (Autolet (R), Owen Mumford Ltd. Oxford, England). 1 – 2 drops of blood making a circle of 1.5 – 2 cm in diameter were dropped on filter paper and left to dry and then stored cool. Filter papers were cut to standard size, giving approxinately 5.0 ul of blood and elluted in Bovine Serum Albumen (BSA), and diluted in dilution buffer to different dilutions before they were tested.

The agglutination test was performed using latex particles coated with toxoplasma antigens (Toxotest MT, (TMT) (Eiken, Japan). Test sera were made to dilutions of 1 :6 to 1 :256 and tested

with the toxotest. Both control positive and control negative sera were included in each plate. To minimize inter – observer error, the Toxotest result was read by one experienced laboratory technician.

Fifty randomly selected serum samples from the pregnant population were subjected to Dye Test (DT) and specific IgM antibodies as a control test and to assess prevalence of active toxoplasma infection in the pregnant women. Specific IgM was tested for by the PHLS Standard enzyme – linked immune sorbent assay (ELISA) for the detection of toxoplasma specific IgM antibody (Balfour A.H., personal communication).

RESULTS:

A total of 459 subjects were screened. Of these, 327 cases were pregnant women, 102 school girls and 30 children. Ages of pregnant women ranged from 15 to 42 years, the majority lie in the 21 – 30 years age group. Out of the 327 pregnant women, incomplete information was obtained from 32 cases and is lacking in 18 cases. There were 206 Libyan and 31 non – Libyan pregnant women of different nationalities.

Fifty sera from the pregnant population were selected randomly (every 10th sample of the list) and subjected for the DT and specific IgM antibodies test.

Antibodies to **Toxoplasma gondii** were detected in 10% of children, 51% of 11 – 20 year age group, 50.2% of 21 – 30 year age group and of 51.7% of above 31 years age group population (table 1).

Out of 327 sera from pregnant women, 164 (50.1%) were positive. Antibodies were detected in

Tabel (1): Seropositivity in different Age Groups to Toxoplasma gondii.

Age Group	No. of Seropositives	(Total No.)	Percentage
0 – 10 years	3 (30)		10
11 – 20 years	Non – pregnant	52 (102)	51
	Pregnant	21 (41)	51
21 – years		106 (211)	50.2
> 31 years		30 (58)	51.7
11 – > 31 years		209 (412)	50.7

Table (2): Frequency of seropositivity in Different Nationalities

Notionality	Positive	(Total No.)	(%)
Libyans	103	(206)	(50.3)
Egyptians	20	(32)	(62.5)
Sudanese	6	(15)	(40)
Palestinian	6	(12)	(50)
Chadi	1	(3)	
Ghana	1	(3)	
Morroco	0	(1)	
Tunisian	1	(1)	
Lebanese	1	(1)	
Madagascar	0	(1)	
Phillipines	0	(1)	

Table (3): Distribution of titres of 50 cases screened by the Dye Test and Toxotest

Dye Test Titres/ Toxo Test Titres	8<	8	16	32	64	128	256	512	Total
16 <	18								18
16	7								7
32			3		1				4
64		2	1	1	1				6
128			2		1				3
256				1	3		3	1	8
<256					3			1	4
Total	25	2	6	2	9	1	3	2	50

103 out of 206 (50.3%) of Libyan and in 37 out of 71 (52.1%) of non – Libyan pregnant women (table 2). Out of 50 sera from the selected pregnant group, 25 were positive by the Dye Test (DT) and 32 by the Toxotest (table 3&4). None of those sera were positive for the specific IgM antibody test indicating that none of these cases had active Toxoplasma infection.

Assuming that the traditional Dye Test (DT) is the most sensitive and specific test (i.e. sensitivity and specificity of 100%) to detect antibodies to **T. gondii**, all cases who had positive titres of 16 by the toxotest and had negative results by the DT were considered negative. So the sensitivity of the toxotext is 100% (25/25) and specificity is 72% (18/25) as tested against the DT (Table 4).

Out of 378 people questioned for the possession of cats, only 47 (12.4%) gave positive answers. Of these 47 cases, 26 (55.3%) had antibodies making only 13.6 of all positive cases. This indicates that there is no correlation between possession of cats and toxoplasma infection.

(Chi – sequare test – (X^2) not significant at 10% significance level).

DISCUSSION:

The screening test used, Toxotest, is easy to do, does not require sophisticated equipment, cheap and found very sensitive (100%) and reasonably (72%) specific when the results were compared with that of the traditional Dye Test.

The prevalence of antibodies to **Toxoplasma gondii** in pregnant women in our study, in Benghazi using this test is 50.1%. This is less than the only figure available (62.3%) for comparison (7). It can be argued that this figure 62.3%, is perhaps misleading as the sample (41 women with history of recurrent abortions) was a selected one and could represent a potential gathering of cases with toxoplasma infection. A prevalence of 50.7% of all adults (i.e. women of child bearing age) is consistent with figures from other countries (2,6,13). In an area in Saudi Arabia the figure reported is very similar, 51.2%, using the same test (1) (Toxotest). The prevalence of antibodies in

pregnant women is also consistent with figures from other countries (2). The prevalence of antibodies in school girls is 51% and this is close to the figure for the pregnant women. The prevalence in children (0 – 10 years) is much less, being only 10%, and the only two seropositive children were older children (9 and 10 years of age). This means that most girls get infected when they reach their teens. Further splitting of age – groups into 5 year period was limited by the small numbers available in some age groups but shows 0% positivity at 1 – 5 years, 11.7% at 6 – 10 years, 40% at 11 – 15 years, 49.5% at 16 – 20 years, 55.8% at 21 – 25 years, 49 years of age, No firm conclusions can be drawn from these figures except that seropositivity tends to increase by age. In humans, the incidence of seropositivity for antibody to toxoplasma increases with increasing age, incidence does not vary significantly between sexes. Slaughter house workers may have an increased risk of acquiring the infection. Transmission by unpasteurized goat milk has been reported (11 , 12). Outbreaks within families are common (9) but there is no evidence of direct human – to – human transmission other than from mother to foetus.

The risk of newly acquired infection in a population of pregnant women (seroconversion rate) depends both on the rate of primary infection in that specific geographic area and on the number of people who have not been previously infected. The reported rates for congenital toxoplasma infection per 1000 live births vary between 1.3 and 6.5 (10).

The figures for the Libyan and non – Libyan women were similar, being 50.3% and 52.1% respectively. Because the numbers of non – Libyan women involved in the study were small further analysis of prevalence of antibodies for each nationality was not possible.

The presence of cats appears to be of primary importance in transmission of the infection in most areas of the world (14). However, high prevalences of toxoplasma infection have been found in locales without cats, and low prevalences have been reported in areas with cats (13).

In our study only 13.6% of all seropositive subjects have cats in their houses, which indicates that in the majority of cases the infection is contracted by indirect ways of transmission, even if we assume that all cats are infected (as a rule only about 1 percent of cats examined are found to be excreting cysts (4). Many ways of transmission of Toxoplasma infection are possible: ingestion of contaminated raw fruit and vegetables, handling of raw meat, ingestion of undercooked meat, or drinking of unpasteurised goat milk (12). Ingestion of undercooked meat is almost unknown in Libya. In fact Libyans generally prefer wellcooked meat. Ingestion of contaminated food stuff is another possibility but unlikely to be the main way of transmission as there are very few cats around, judging by the number of people having cats. Indirect contamination of food could be brought about by the dusty wind Giblies: (Seasonal dust – laden winds are a special feature of weather in Libya) carrying oocysts from dried cat faeces as faecal cysts survive outside cats body and the enviroment can be contaminated for very long periods, often a year or more (33). But transmission of infection by ingestion of contaminated food is probably not enough to explain our findings, as the infection is less prevalent among children although contaminated food stuff is more likely ingested by children than adults. One possible way of transmission is contamination of hands by infected raw meat. This could explain the high prevalence in adult women and school girls and the low prevalence in children, as children are very unlikely to handle raw meat. It is a very common practice that these adolescent girls help their mothers in the kitchen. The high prevalence of infection in the absence of well – known ways of transmission suggests that other factors are involved, among these Christie suggested, droplet infection as cysts have been demonstrated in the alveoli of infected animals, and so might be present in man's sputum (34).

The prevalence of antibodies to **T. gondii** in pregnant women in Benghazi is 50.1%. These women are presumed immune and are at no risk of getting infected during pregnancy. The other half are seronegative and susceptible to infection which

if contracted during pregnancy could lead to congenital toxoplasmosis and foetal morbidity. The risk of contracting toxoplasma infection during pregnancy depends on the infection rate in the community and on the number of susceptible individuals (i.e. seronegative people). Infection rate for toxoplasma in Benghazi is not known, neither is the seroconversion rate for pregnant women. To answer these questions and other questions raised during discussion, we need to continue this kind of research at different sites and at different trimesters.

Table (3): Distribution of age and the proportion of seropositive case, at each titre.*

Age Group/ Titres	0 – 10	10 – 20	21 – 30	> 31	Total
< 16	25	54	69	16	164
16	3	15 (17.2%)	40 (27.2%)	13 (30.9%)	71
32		8 (9%)	13 (9%)	6 (14.3%)	27
64		12 (13.8%)	15 (10.5%)	7 (16.6%)	34
128	1	25 (28.7%)	19 (13.2%)	4 (9%)	49
256		17 (19.5%)	33 (23.7%)	6 (14.3%)	56
> 256	1	10 (11.5%)	23 (16%)	6 (19.3%)	40
Total	30	141	212	58	441

(*) Positive when titres are 16 or above.

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Pseudo -Tumour Cerebri : Incidence and Pattern in North - Eastern Libya

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(Received in 14 .11 .1992)

SUMMARY

Twenty four patients with pseudotumour cerebri were seen over a period of one year. There were 20 female and 4 males. This constitutes an annual occurrence of 4.1/100,000 for the general papulation and 19.5/100,000 for females aged 11 to 44 years in the Banghazi area. The female to male ratio was 5 :1 , and mean weight was 70% above the ideal weight for the female.

Moderate to severe visual loss occured in 25% of patients. Pseudotumour cerebri is a relatively common neurological illness and may be an important preventable cause of blindness in obese young women. We found that repeated lumbar puncture was much more beneficial, at the early stage, in alleviating the symptoms and promoting better outcome.

الملخص

شخصت في فترة واحدة أربعة وعشرون مريضاً بورم المخ الوهمي (عشرون أنثى وأربعة ذكور). وبهذا تكون نسبة الحدوث السنوي في منطقة بنغازي 4.1/100 000 لمجموع السكان الكلي، و19.5/100 000 للإناث بين سن 11 – 44 سنة، نسبة الحدوث في الإناث إلى الذكور هي 5: 1 ، وكان متوسط وزن الجسم في الإناث 70% أعلى من الوزن النموذجي، وحدث فقدان نظر من متوسط إلى شديد في 25% من هذه الحالات.

ورم المخ الوهمي يعتبر مرض عصبي شائع نسبياً وقد يكون سبباً هاماً. وقابلاً للعلاج لفقدان النظر في النساء زائدات الوزن في مقتبل العمر. وقد وجد أن للنخسة القطنية المتكررة فائدة في مرحلة المرض الأولى في تخفيف الأعراض وتحسين النتائج النهائية.

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INTRODUCTION:

Pseudotumour cerebri may be defined as a syndrome of elevated intracrani alpressure without clinical, laboratory or radiologic evidence for focal lesions or hydrocephalus. Four criteria must be fulfilled to make the diagnosis of pseudotumour cerebri (PTC):

(1) documented elevation of intracranial pressure (> 200 mm water).

(2) normal cerebrospinal fluid (CSF) composition;

(3) normal neurologic examination results except for papillaedema and VI nerve palsy; and

(4) normal results of neuroimaging studies (computed to tomography showing normal of small – sized ventricles).

The symptoms of PTC are related to the elevated intracranial pressure (7). Headache, visual symptoms, and diplopia are the most common. Papillaedema and paresis of the VI nerve are signs of increased intracranial pressure. Focal neurologic signs suggest some other diagnosis.

In this study our aim is to find out the frequency, causes and patient characteristics among the Libyan population.

MATERIALS AND METHODS

Patients with pseudotumour cerebri admitted to «7th April» Hospital, Benghazi during a one year period (January 1991 to December 1991) were the subjects of this study. This is a referral hospital affiliated to Al Arab Medical University and only this hospital provides neurology services to the whole north – eastern sector of Libya. Case records of all patients with PTC were studied and reviewed for multiple variables including age, sex, race, height, weight, evidence of hypertension, blood cell count, protein determination, and pregnancy status. Thyroid abnormalities, history of systemic lupus erythematosis and other connective tissue disease were also inquired. A history of medication intake, such as contraceptive pills, vitamins, vitamin A, steroids and nalidixic acid, was obtained. Diagnostic criteria included evidence of papillaedema, increased CSF pressure, normal CSF protein values and normal neuroimaging studies.

Physical signs and symptoms at the time of diagnosis were reviewed with special emphasis on the following: headache, visual symptoms (visual loss, blurring, transient visual obscuration or diplopia), papillaedema and VI nerve paresis. Hypertension was defined when medication was required for high blood pressure or when blood pressure was greater than 150/90 mm Hg on three occasions using the appropriate sized cuff. Obesity was defined as weight more than 20% over the ideal weight. All the patients had computed tomography scan.

RESULTS

Twenty four patients fulfilled the criteria of PTC. There were 20 (83%) females and 4 (17%) males (female to male ratio of 5 :1). Patien ages ranged from 11 to 44 years (mean 28.5 years). The women ranged in age from 11 to 36 years. The mean weight was 70% above the ideal weight (ranging from 20% to 80% above the ideal weight for female). One female was pregnant when diagnosed, and 2 females used oral contraceptive pills.

The population of Benghazi area in 1991 was 583,575. There were 102,165 females between the ages of 11 and 44 years and 137,651 males in the same age group. Thus, the one year occurrence of PTC in the general population of Benghazi areas was 4.1/100,000 persons. The frequency in females and males aged 11 to 44 years were 19.5/100,000 and 2.9/100,000 respectively.

Twenty three patients (95.8%) had headache as their only presenting symptom (Table I). 19 patients (79%) had a combination of headache and visual symptoms. During the active phase of their condition, 24 patients (100%) complained of headache, 17(70.8%) suffered from visual symptoms, 17 (70.8%) had TVOs, 6(25%) had visual loss, and 4(16.6%) had diplopia. Papillaedema was seen in all patients. VI nerve palsy was recorded in 4 patients (16.6%), enlarged blind spot in 3 (12.5%) and decreased visual acuity in 6(25%).

The mean interval from data of onset of symptoms to data of diagnosis was 7.9 months; ranging from less than one month to 36 months. History of medication intake revealed that one patient took daily multivitamins. Another patient was taking atenolol for her hypertension.

All patients had undergone repeated lumbar punctures; every 2 days to every week upto 30 ml of fluid was drawn off to lower the intracranial pressure. Most of our patients had experienced improvements in their clinical state.

All patients were also given acetazolamide, in addition to repeated lumbar puncture.

DISCUSSION

Pseudotumour cerebri is considered an uncommon disease. Rush (8) described 63 cases seen at Mayo Clinic between 1961 and 1978 . One hundred and twenty four patients were seen with PTC at Killean Hospital in Glasgow, Scotland, between 1942 and 1972 (5). Wall et al (9) reported 48 cases at washington University, St. Louis, from 1974 to 1980 . To determine the incidence of PTC is not common. We attempted to determine the incidence of PTC in Benghazi area to determine the characteristics of the population at risk and to calculate the incidence of PTC. An annual incidence of 4.1/100,000 persons in the general population and 19.5/100,000 in females from 11 to 44 years of age was calculated. In men aged 15 to 44 the incidence of 209/100,000 was reported. Our results are higher than the figure reported earlier by Radhakrishana et al (7) from Benghazi are, but comparable with published incidence data from lowa (4) where an annual incidence of 19/100,000 in obese women of the same age group, 20% or more over the ideal weight is reported.

There is widespread agreement that PTC is more common in women than it is in men. It is confirmed in our study, where the female to male ratio was 5 :1 . Although this ratio has been reported as low as 1.8 :1 (5), there are also reports in which all the patients were females (7).

The patients in our study ranged in age from 11 to 44 years, which is in agreement with other reports (9). In earlier studies, headache was reported in 52% as compared with 95% in our study, and TVOs were reported in 26% of reported cases vs. 70% in our study. Papillaedema was seen in 95.8% of the cases reported in the literature in 11% of the cases, which is comparable with our result (16.6%) In our study, there was moderate to severe visual loss in 25% of cases compared with some data by Corbett (2). The incidence and extent of visual impairment did not correlate with duration of symptoms, degree of obesity, use of contraceptive pills, degree of papillaedema, visual obscuration.

Obesity is a significant factor in this syndrome and is reported to occur from 11.1.%(7) to 90% of cases (9). Seventy per cent of our patients were obese. The exact role of obesity in the pathogenesis of PTC remains unclear. Pseudotumour cerebri occurs during pregnancy. Digre et al (3) found that pregnancy occured in patients with PTC at the same rate that it occurs in the general population. We found that 5% of our female patients were pregnant.

Oral contraceptive use has been associated with PTC. 12% of our female patients were using contraceptives, 15.6% of the female population between 16 and 44 years old use contraceptive pills. There is no significant difference between our population of patients with PTC taking contraceptive pills and the general female population taking the pill. Digre et al (3) also found no significant difference in oral contraceptive use between patients with PTC and their controls.

Many medications have been implicated in the pathogenesis of PTC. One of our patients took daily multivitamins. One patient took Vitamin A supplements. The relationship between Vitamin A and PTC has long been established. Vitamin A products, ketoprofen, indomethacin, tetracyclines, lithium carbonate and nalidixic acid should be inventoried when taking the history of medications. The association of tetracycline is well known; none of our patients were taking tetracyslines.

The role of corticosteroids, causing or exacerbating PTC, was reported in the medical

literature. None of our patients were taking steroids.

Pseudotumour cerebri has been associated with both primary and secondary hypoparathyroidism (9). None of our patients had hypopara – thyroidism.

Hypertension may be a risk factor in PTC (7). One of our patients had hypertension. Serial lumbar punctures do have a place in the treatment of patients with pseudotumour cerebri, at the very least, serial lumbar puncture appears to be useful early in treatment as shown with our patients. Twenty eight of Weisberg's patients (10) had this as the sole from the therapy. It was continued for up to one year, by which time 26 patients had experienced remissions.

The incidence of PTC in the general population and in the population at risk was calculated from the symptomatic group. We confirmed earlier observations that this disease tends to occur in obese women of child – bearing age. Severe visual loss has been shown to occur in up to 25% of patients with PTC (2).

In view of these observations, we believe that PTC represents an important risk to vision in obese young women.

Table (1) : Frequency of symptoms and signs of presentation in 24 patients.

Symptoms	No. of Patients	(%)
Headache	23	(95.8)
Transient visual obscuration	17	(70.8)
Visual Loss	6	(25.1)
Diplopia	4	(16.6)
Nausea	1	(4)
Tinnitus	1	(4)
SIGNS		
Papilledema	24	(100)
Sixth Nerve Palsy	4	(16.6)
Enlarged Blind Spot	3	(12.5)
Decreased Visual Acuity	6	(25)

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Incidence of Non-Insulin - Dependent Diabetes (Type 2) in Benghzai , Libya (1981 - 1990)

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SUMMARY

The overall mean annual incidence of non – insulin dependent diabetes mellitus (MIDDM type 2) in Benghazi based on prospective registration of patients during the period 1.1. 1981 to 31. 12. 1990 was 0.193/100 population (males 0.171/100, females 0.215/100). The incidence rate rose with age and peaked in 50 – 54 years age group in both sexes.

The incidence rate was significantly higher in females ($p < 0.01$).

It was concluded that after the control of endemic diseases, diabetes mellitus is emerging as a major health problem in Libya.

الملخص

في دراسة مخططة من واقع سجلات المرضى، حسبت نسبة وقوع الداء السكري الغير معتمد على العلاج بالأنسولين (النوع الثاني) في بنغازي، في الفترة من 81/1/1م وحتى 90/12/31م.

وقد وجد أن نسبة الوقوع العامة لهذا الداء في بنغازي كانت 0.193 لكل 100 من السكان (رجال: 0.161 لكل 100 ، نساء: 0.215 لكل 100).

وارتفعت نسبة الوقوع مع التقدم في العمر.. ووصلت قمتها في المجموعة العمرية 50 إلى 54 سنة في الجنسين. وهكذا يتضح أن الداء السكري، بعد أن تم التحكم في الأمراض المتوطنة، قد يصبح من أهم المشاكل الصحية في ليبيا.

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INTRODUCTION:

There is abundance of data about the incidence of insulin dependent diabetes mellitus (IDDM Type 1). But there are far less studies of the incidence of non – insulin dependent diabetes mellitus (NIDDM Type 2) from developing countries. We have reported the clinical characterisics of diabetes mellitus in Benghazi (4,5).

This paper presents the incidence of type 2 diabetes in Benghazi, Libya, in ten years (1981 – 1990).

PATIENTS AND METHODS

Benghazi municipality is the second largest municipality in Libya (5,75,000 inhabitants). Benghazi diabetic clinic, established in 1969 , is the only diabetic clinic in Benghazi municipality. It is a daily outpatient clinic with an average daily attendance rate of 150 – 250 patients. public pharmacies and outpatient clinics, they are available only in the diabetic clinic (free of charge) and in hospitals for inpatients. All known diabetic patients in the area must register to get their insulin and oral hypoglycaemic agents. All patients are Arabs of whom 5 – 10 percent are non Libyan Arabs.

All registered patients have files and personal diabetic cards. Diagnosis and classification of patients into Type 1 and Type 2 are based on World Health Organization criteria (9). A patient is considered insulin dependent if he or she is ketosis

Table (1) : Incidence (per 100,000) of non insulin dependent diabetes mellitus (Type II) in Benghazi (1981 – 1990). **(Number of cases given in Parenthesis)**

Age Group	Males	Females	Total
0 – 9	0 (0)	0.1 (1)	0.06 (1)
10 – 19	3.2 (18)	4.0 (22)	3.6 (40)
20 – 29	44.7 (165)	67.4 (237)	55.8 (402)
30 – 39	270.4 (609)	581.0 (1249)	422.0 (1858)
40 – 49	754.8 (1201)	997.3 (1479)	996.3 (2680)
50 – 59	1195.0 (1269)	1225.0 (1176)	1209.2 (2445)
60 – 69	988.0 (576)	1028.3 (582)	1007.8 (1158)
70 +	874.1 (243)	679.4 (195)	775.2 (438)
Mean Annual Incidence	170.8 (4081)	215.3 (4941)	192.6 (9022)

prone without insulin therapy since diagnosis, otherwise he/she is considered non- insulin dependent.

The incidence data are based on prospective registration of patients in ten years, from January 1 , 1981 to December 31 , 1990 . The incidence rates are presented in 5 and 10 years increments with sex stratification. The number of residents per sex and 5 year age group for the years 1981 to 1990 were obtained from the National Census Bureau in Tripoli. Incidence was calculated from the members of new cases in each age group divided by the numbe. of population at risk in each year. The mean annual incidence rate was calculated in the total number of new cases in ten years in each age group divided by the total number of population at risk. An ordinary $\times 2$ was applied to test the significance of difference. The criterion for significance was P value < 0.05.

RESULTS

Of the total 15213 patients (males 6835, females 8378) registered at the end of 1990 , 24650 patients (males 6520, females 8130) were Type 2 patients (96.3 percent). Malnutrition- related diabetes was not observed in Benghazi. During the study period (1981 - 1990), 9022 Type 2 patients (males 4081, females 4941) were registered. The overall mean annual incidence was 0.193/100 population (males 0.171/100, females 0.215/100) (tables 1, 2). The incidence rate rose with age and peaked in 50 - 54 years age group in both sexes. The mean annual incidence was significantly higher in females ($P < 0.01$).

DISCUSSION:

It is difficult to ascertain the incidence of Type 2 diabetes in a population. Serial systematic studies using World Health Organization criteria should

Table (2) : Incidence (per 100,000) of non- insulin dependent diabetes mellitus (Type II) in Benghazi (1980 - 1990). **(Number of cases given in Parenthesis)**

Age Group	Males	Females	Total
0 - 4	-	-	-
5 - 9	0.0 (0)	0.3 (1)	0.1 (1)
10 - 14	1.6 (5)	2.3 (7)	1.6 (12)
15 - 19	5.0 (13)	6.0 (15)	5.5 (28)
20 - 24	23.7 (50)	27.7 (56)	25.6 (106)
25 - 29	72.8 (115)	121.1 (181)	96.3 (296)
30 - 34	168.7 (212)	377.1 (442)	269.2 (654)
35 - 39	398.9 (397)	825.1 (807)	610.2 (1204)
40 - 44	631.2 (553)	954.3 (772)	786.4 (1325)

Age Group	Males	Females	Total
45 – 49	906.2 (648)	1076.1 (707)	987.6 (1355)
50 – 54	1313.6 (802)	1597.8 (859)	1446.8 (1661)
55 – 59	1008.8 (467)	749.4 (317)	894.9 (784)
60 – 64	1096.2 (376)	1303.7 (425)	1197.3 (801)
65 – 69	833.3 (200)	654.1 (157)	743.7 (357)
70 +	874.1 (243)	679.5 (195)	775.2 (438)
Mean Annual Incidence	170.8 (4081)	215.3 (4941)	192.6 (9022)

be performed on a fixed population to estimate a valid "true" NIDDM incidence.

Serial systematic studies using World Health Organization criteria have been performed on the Pima Indians of Arizona, Micronesians and Maltese diabetic population. The Pima Indians have Type 2 diabetes incidence of 1.85 per 100 person years at all ages (6). For Micronisians the incidence rate is 1.54 at all ages (3, 10). The incidence rate of Type 2 diabetes in Malta is 0.71/100 person years (7). In the United States of America, Bender et al (2) reported Type 2 diabetes incidence of 0.117 per 100 population for three communities in Minnesota, based on physician – diagnosed diabetes. This is in line with previous peport of 163 per 100 person years in Rochester, Minnesota during the period 1960 – 1969 (6).

In Europe the age standardised mean annual incidence of diabetes ranged from 0.331 per 100 population in Laxa municipality in Sweden (1) to. 0.069 per 100 population in Scotland (8).

In Benghazi few asymptomatic Type 2 diabetes may not register in the diabetic clinic. Another source of bias is that few patients from outside Benghazi may register in Benghazi diabetic clinic. For these reasons we did not comment on yearly fluctuations and seasonal variations of incidence.

The incidence rate in the current study is intermediate between the lower rates reported from the United States of America and Scotland, and the higher rates reported from Malta and Sweden and substantially lower than the incidence rates of Pima Indians and Micronesians. The incidence rate in the current study was low in children and adolescents increased with age and peaked in 50 – 54 years age group and then declined. In affluent societies the frequency of Type 2 diabetes rises with age and peaks in 70 – 79 years age group (8).

In contrast to affluent societies the incidence rate in the current study was more frequent in females.

CONCLUSION:

It is evident that after the control of endemic diseases in Libya (Tuberculosis, schistosomiasis, malaria, trachoma and leprosy), diabetes mellitus is emerging as a major health problem. Diabetes mellitus has been considered a priority in health planning in Libya. A national committee for

diabetes is existing since 1982 . Diabetic patients all over the country are registered and treated in diabetic centres and diabetic clinics. Diagnosis and classification of diabetes mellitus are based on World health Organization recommendations. Diagnostic facilities, highly purified and human insulins and insulin syringes are free of charge. Epidemiological research is encouraged by Secretariate of Health, medical schools and the Libyan Medical Research Council.

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Prevalence of Salmonellosis among Infants and Children in Benghazi during a Two - Month Period

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SUMMARY

Forty eight isolates of Salmonella species were found from 255 stool samples obtained from infants and children with diarrhoea, admitted to the children's hospital in Benghazi, Libya during a two – month period. Of the children studied, 18.8% were from infected infants under one year of age. Fifteen percent of children between 1 – 2 years of age were infected with Salmonella and similar percentage rate. Approximately 2 :1 male to female ratio was noticed among the infected children. Most of the isolates appeared to be resistant to chloramphenicol, ampicillin and other antibiotics used but sensitive to smoxtcillin – clavulanic acic (Augmentin).

الملخص

في دراسة استغرقت شهرين، تم عزل (48) نوعاً من جرثومة السالمونيلا الغير تيفودية من مجموع (255) عينة براز من مرضى أطفال مصابين بالاسهال وأدخلوا للعلاج في مستشفى الفاتح لطب وجراحة الأطفال. بهذا تكون نسبة إنتشار العدوى السالمونيلية فيهم 18.8%، حدث منها 40% في أطفال دون السنة الواحدة من العمر، بينما كانت النسبة 15% من الأطفال بين عمر 1 – 2 سنة، ومثلها في الأطفال بين عمر 2 – 3 سنوات، وكذلك 3 – 4 سنوات، كانت نسبة الاصابة من الذكور إلى الإناث 2 إلى 1 على التوالي.

بعد إجراء اختبارات الحساسية للمضادات الحيوية المستعملة في علاج هذه العدوى، وجد أن معظم الجرائيم التي عزلت من المرضى تقاوم عقار الكلورامفينيكول والأمبسلين، ولكنها حساسة للأوجمانتين.

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INTRODUCTION:

Salmonellosis is a disease that can occur both in humans and animals. There are more than 2000 serotypes of Salmonella (6). Of these, Salmonella typhi and Salmonella paratyphi A, B and C are restricted to man and cause enteric fever. Other serotypes are of animal origin, and cause zoonotic disease in humans, that are mainly confined to the gastrointestinal tract. Infection with these serotypes occur as a result of ingestion of contaminated food and water (4, 6). These non – typholid Salmonellae are considered the common causative agents of bacterial food poisoning worldwide but in particular, in developing countries.

We have investigated the incidence of such Salmonella infections in infants and children in The Children's Hospital, Benghazi. The sensitivity of these Salmonella isolates to the commonly used antibiotic was also tested. The results are discussed in this paper.

MATERIALS AND METHODS

Two hundred and fifty five stool samples were collected from infants and children admitted to the Children's Hospital in Benghazi with variable symptoms of diarrhoea, abdominal pain and fever, during the period from July 1st to September 1st, 1992 .

Each stool sample was inoculated onto xylose – lysine deoxycholate (XLD) agar and into selenite F broth. The plates and tubes were incubated at 37 C for 24h. Pink colonies with black centers grown on the agar plates were isolated and incubated on McConkey agar for further investigations. Subculture from selenite F broth onto McConkey agar was done when no growth appeared on XLD.

Single colonies isolated from XLD agar were tested for urease activity in Christensen's urea medium. Urease negative isolates were inoculated onto triple sugar iron (TSI) slopes and incubated at 37 for 24h.

Preliminary identification of the isolates was done by slide agglutination test using Salmonella somtic agglutinin serum developed in rabbit (Wellcome, U. K.). Agglutination appeared within one minute. Controls were bacterial suspensions with no antiserum to detect spontaneous agglutination. Positive cultures were further identified by biochemical tests using the API 20E system (Bio Merieux, France).

Antibiotic sensitivity tests were carried out for each isolate by the Kirby – Bauer technique using agar. No.1 (oxoid). The following antibiotic discs were used: Ampicillin (10 Mg), Amoxycillin – Clavulanic acid (augment in 10 Mg), Cephalaxin (5 Mg), Cotrimethoxazole (25 Mg), Chloramphenicol (10 Mg), Tetracycline (10 Mg), Gentamicin (10 Mg) and Kanamycin (30 Mg). After 24th incubation at 37 C, zones of inhibition of growth were measured and compared with those produced by the control strain (E. coli, NCTC 1160).

RESULTS

Salmonella species were isolated from 48 samples out of the 255 stool samples examined (18.8%). Table 1 shows the number of these samples and per cent isolation during the various weeks in the months of July and August. The isolates were urease negative, and on TSI agar all produced alkaline slants, acidic butts with H2S and many with gas production. The API 20E system identified all these isolates as Salmonella species (but could not determine the exact species) and excluded Salmonella typhi, S. paratyphi A and S. paratyphi B. Exact identification of these isolates into species by other tests was not possible due to shortage in the reagents required.

It was found that around 40% of the children infected were under one year of age (ranging between one month and eleven months of age) (table 2). Approximately 15% of infection occur in children between 1 – 2 years of age and similar infection rates were noticed in those between 2 – 3 years children over 4 years age group. Male children were found to be more infected with Salmonella than female children, representing a ratio of approximnately 2:1 .

Antibiotic sensitivity test results (table 3) showed that many isolates were resistant to

chloramphenicol and ampicillin and to most other antibiotics tested while many of them were sensitive to "augmentin" only.

DISCUSSION

Acute gastroenteritis can occur as a result of ingestion of food (mainly chicken, meat and eggs) and water contaminated with bacteria from faecal material either directly or indirectly. Such bacterial infection is commonly due to contamination with different Salmonella serotypes (3). Among nearly 2000 serotypes known, the most commonly isolated worldwide are Salmonella entritidis, S. typhimurium, S. virchow, S. hadar, S. heidelberg, S. agona and S. indiana (6).

The predominance of either of these serotypes is variable. Shifting occurs in a constant manner from one year to another and in different areas of the world. In one report, S. typhimurium was the predominant cause of gastroenteritis in Hong Kong up to 1971 , then S. Johannesberg suddenly dominated in 1972 until 1977 . This was attributed to the increase in food stuff imports from other countries during that period (5). In Britain, it was found that S. typhimurium predominate in children with gastroenteritis (3, 4, 7).

In a previous study done in the same children's hospital in Benghazi during the period 1977 – 1980 , non – typhoid Salmonellae were isolated from 150 bacteriologically confirmed cases and found to belong to S. muenchen group C2 (80.74%), S. bovis – morbificans (16.69%) and S. senftenberg (1/48%) (1).

In our report, the results obtained from the API 20E data profile confirmed that the isolates were Salmonella species. The API 20E system has its limitations in further identification of the non – typhoid Salmonellae, however this was considered useful since it excluded the typhoid and paratyphoid Salmonellae.

In our study an 18.8% infection rate was recorded. Such high prevalence of infection at this hospital does seem to be due to the persistance of Salmonella species in the hospital premises, and possibly carried by health personnel since in a previous study done at the same hospital, the investigators were able to isolate Salmonella species from premises in all hospital wards from two of the nursing staff (1).

We have found that infants under one year of age were more prone to infection than elder children. Although Salmonella can infect humans at any age, higher susceptibility to infection in infants may be attributed to contamination during bottle – feeding, especially in hospital, as well as immaturity of the defense mechanisms, poor hygiene and socioeconomic status. Similar findings were reported by Elliott et al (1988), when 66% of children infected with Salmonella were under one year of age, and by Abudejaja al (1982).

Higher incidence of infection was noticed in our study in male infants and children than in a ratio of approximately 2 :1. Similar observation was peported by Elliott et al (1988). Whether genetic factors play a role in susceptibility to such infections is still not known. However, Abudejaja et al (1982) reported no significant differences in infection rates between males and females.

Lui et al (1979) reported that the highest incidence of diarrhoea in patients occured between the months of July and September. However, Abudejaja et al (1982) reported variable incidence rates during their three years investigation period. The hot weather during the summer months may still play an important role in such incidence since it favours the growth of Salmonella organisms.

Antibiotic sensitivity tests revealed that most of the isolates were resistant to the commonly used drugs for treatment of Salmonellosis, such as gentamicin, chloramphenicol and ampicillin. Resistance of non – typhoid Salmonellae to such drugs was reported (6). The rising resistance among Salmonellae has been related to the common practice in the use of antibiotics in farm animals and in human infections. However, earlier reports (1, 8) from Benghazi, showed higher sensitivity of Salmonella species to the main antibiotics tested. The increase in resistance since may be due, at least in past, to the non – judicious use of antibiotics and the lack of an antibiotic policy. Generally, treatment of Salmonella

infections with antibiotics is not recommended and is given only for individuals at risk of severe disease or septicaemia (6). The majority of the isolates were sensitive to augmentin (89.6%). This antibiotic is not commonly used in this area, and is a recently applied antibiotic.

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Table (1) : Prevalence of Salmonella spp. detected in the Children's hospital, Benghazi during two months investigation period.

	Jul (Week)				August (Week)				Total
	1st	2nd	3rd	4th	1st	2nd	3rd	4th	
No. of stool samples examined	12	31	48	44	29	34	30	27	255
No. of Salmonella positive samples	2	10	6	10	5	8	5	2	48 (18.8%)

Table (2) : Distribution of 48 infected children with Salmonella species according to their age groups and sex.

Age (Years)	Male	Female	Total	% Infected
1	12	7	19	39.6
1 –	4	3	7	14.6
2 –	5	3	8	16.6
3 –	5	2	7	14.6
4 –	2	1	3	6.3
5 –	2	–	2	4.1
6 –	1	1	2	4.1
Total	31	17	48	100.0

Table (3) : Antibiotic sensitivity pattern of 48 Salmonella species isolated from faces of infected children

Antibiotic Disc	No. Of Isolates	
	Sensitive	Resistant
Augmenti (10 Mg)	43 (89.6)	5 (10.4)
Tetracycline (10 Mg)	27 (56.3)	21 (43.7)
Gentamicin (10 Mg)	14 (29.2)	32 (70.8)
Cephalexin (5 Mg)	13 (27.1)	35 (72.9)
Chloramphenicol (10 Mg)	12 (25.0)	36 (75.0)
Cotrimethoxazole (25 Mg)	10 (20.8)	38 (79.2)
Ampicillin (10 Mg)	7 (14.6)	41 (85.4)
Kanamycin (30 Mg)	6 (12.5)	42 (87.5)

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Incidence and Pattern of Cleft Lip and Palate in Benghazi (G.S.P.L.A.J) A Five Year Retrospective Study (1984 - 1988)

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SUMMARY

A five years (1984 – 88) study of cleft lip, with or without cleft palate, malformation was conducted based on the records of the maternal unit and neonatal unit of "Al Jamahiriya" hospital, Benghazi. A total of 22 cases of cleft were noted among 76 , 406 live Libyan births during the study period, giving in incidence of one in 3,473 live births among infants of benghazi (Libya), which is low when compared with other studies. The most frequent type of cleft in this study was bilateral and median cleft lip and palate. A common associated congenital malformation was facial anomaly. A high proportion of cleft cases was observed at a young maternal age, between gravida 1 – 3 , and in infants of maternal blood group O + and also in low birth weight (2, 500 gms) and preterm (37 weeks) babies.

الملخص

إن دراسة تشوهات الشق الخلقي بالشفاه والحلق للسنوات الخمس التالية (1984 – 1988) بمدينة بنغازي من خلال سجلات الولادة وحديثي الولادة بمستشفى الجماهيرية بيّنت أن عدد هذه الحالات 22 حالة من أصل 76.406 مولود ليبي خلال هذه السنوات الخمسة.

وهذه النسبة تعتبر الأقل مقارنة مع الدراسات الأخرى التي أجريت بهذا الصدد.

وكان أكثر الأنواع انتشاراً من هذا التشوه هو الشق الخلقي بالشفاه والحلق معاً ذو الجانبين أو الوسطى وأكثر التشوهات المرافقة له هي تشوهات وجهية أو بالوجه.

وقد لوحظ أن أكثر حالات التشوهات الخلقي بالحلق قد سجلت لأمهات صغيرات السن، وعدد ولادات مبكرة، وفصيلة دم (O+) كما لوحظ أيضاً أنها سجلت لمواليد ذوي أوزان صغيرة.

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INTRODUCTION:

Estimates of the frequency of cleft lip with without cleft palate malformations range from 0.8 to 1.6 per 1,000 live births in various reliable studies (1,3,5,6). In a recent large study sponsored by WHO on hospital births, the range was from 0.6 in czechoslovakia to 1.52 in Santiago Chile (9,14). The frequency was higher in caucasians (1.34 per 1000 births) than in American Negros (0.44 per 1000) and higher in Japanese (2.13 per 1000) and Malayans (1, 13, 14).

These variation may represent differences in the racial frequencies or in geographical variations, in reporting.

Knowledge of the etiology of cleft lip and cleft palate is still deficient and confused. Multi – factorial genetic inheritance and environmental factors have been considered to be of etiologic significance. A relatively small number (3 percent) may have one or more additional structural abnormalities or have identifiable syndromes or associations. The factors underlying cleft lip with or without cleft palate can be considered in four categories: 1 . Mutant genes, 2. chromosomal aberrations, 3.Environmental teratogens and 4 .Multifactorial inheritance.

There is a complete lack of information regarding the frequency, pattern, associated anomalies, and associated factors, with cleft lip, with or without cleft palate, malformations in Benghazi (Libya). The present study is the first in this direction in the region and this study will also establish a baseline for national and international comparison.

MATERIAL AND METHODS:

The sources of data for the present study included records of the maternity unit and neonatal unit of "Al Jamahiriya" hospital, which is a teaching and referral hospital. All births for the five year period (184 – 1988) were recorded. 22 cases of clefts were diagnosed during that period. They are classified according to the classification given below. Maternal factors; viz. maternal age, maternal blood group, maternal gravida, gestation period, birth weight and association with other congenital anomalies were recorded as per proforma (enclosed) and analysed in reaction to all cases of cleft lip with or without cleft palate.

RESULTS AND DISCUSSION:

The Al – Jamahirya hospital is the only maternity hospital for the whole municipality of Benghazi. It caters for not less than 90% of total deliveries in the area (10). A total of 22 clefts were noted among 76,406 live births during the period of five years (1984 – 1988), giving an incidence of one in 3,473 live births, indicationg risk of cleft malformation among infants of Benghazi (Libya). Table (1) shows yearwise incidence of clefts, wich

Basic Cleft Palate Classification (2):

		Left	Median	Right
Prepalate or Primary Palate	Lip			
	Alveolar Process			
		Incisive Foramen		
Palate or Secondary Palate	Hara Palate			
	Left			Right

was highest (5.2 per 10,000 live births) in 1986, followed by 3.22 per 10,000 births in 1988 . Table (2) compares the incidence of clefts in Benghazi (Libya) with the incidence in various other countries and racial groups. The frequency of cleft lip with or without cleft palate ranges from 0.8 to 1.6 per 1000 live births. However, in the present series it is 0.28 per 1,000 live births which is quite a low frequency. These variations may represent differences in the racial frequencies, in geographical variation, in teratogenic factors or in reporting. An equal incidence between sexes was found in the present study, however, in certain other studies, a slight excess of males with cleft have been observed.

Pattern of Cleft

Table (3) shows the most frequent type was to be bilalteral and median cleft lip and palate which constituted 6 cases (27 percent) each. Unilateral left cleft lip and palate (22.7 percent) was more common than right cleft lip and palate (13.6 percent). There were 7 cases of cleft palate alone but there was none of cleft lip alone. similar distribution of clefts in the new born have been observed by other studies (8, 12). Cleft lip and palate and isolated cleft (2, 4). There are embryologic and genetic grounds to suggest that cleft lip, and cleft lip with cleft palate, represent variations in the severity of some developmental defect.

Associated Anomalies:

A list of associated congenital malformations is shown in Table (4). Ten (45.45%) cases were associated with facial anomalies and 6 cases of Downs Syndrome associated with mental retardation, congenital heart disease, macrocephaly and Rocher bottomfeet (Trisomy 13, 18). Four cases were of multiple congenital anomaly. Piere Robin Syndrome was identified in 2 cases.

It is characterised by micrognathia, glosoptosis and cleft palate. Various estimates for associated congenital malformations range from 10 to 20 percent (3,6,7,13).

Associated Maternal Factors:

Association of frequency of cleft malformation was analysed for certain maternal factors such as maternal age, gravida, blood guoup, period of gestation, and birth weight which are shown in Table 5 (A,B,C,D & E). High proportion (54.54%) of clefts were observed at young maternal age (20 – 25 years) and in gravida 1 to 3 . In a number of studies some association of cleft lip, with or without cleft palate, have been reported with advancing parental age, particularly that ot the father (3, 11). For the present study father's age was not available on the records and also absent was the information regarding consanguinity.

Although higher proportions of cleft cases were found with the maternal blood groups O+, B+ and A + ve (Table 5 C) but, when the frequency of cleft was calculated according to the distribution of blood groups in the mothers, there was no excess of cleft frequency according to maternal blood group. The frequency of cleft was 1.17 per 1000 low birth weight babies and was 0.66 per 1000 preterm babies, indicating excess of risk among low birth weight and preterm births.

Seasonal Variation:

Accurate dates of birth were obtained in all 22 patients (Table 6). No consistent variation in the frequency of cleft lip or cleft palate with season of birth was observed. However more of the affected children were born from February to April. If the last menstrual period (L.M.P.) is calculated by counting back nine months, then births in February to April correspond to June to August. It would be interesting to study possible relationship between increased frequency of clefts during these methods.

Tabel (1) : Shwing yearwise incidence of cleft

Year	Total Live births (Libyan)	No. with cleft	Incidence per 10,000 live births
1984	15,482	4	2.58
1985	15,156	3	1. 97
1986	15,348	8	5.21
1987	14,924	2	1.34
1988	15,496	5	3.22
Total	76,406	22	2.87

Table (2): Showing comparison of cleft frequency in various countries

S. No.	Country/ Place	Year	Base Population	Cleft per 1000
1.	England	1960 – 82	L.S.	1.40
2.	Finland	1972 – 73	L.	1.63
3.	U.S.A. (New York City)	1972	L.	0.98
4.	Australia	1963 – 72	L.	1.73
5.	Japan	1956	L.S.A.	1.94
6.	Nigeria	1976 – 80	L.	0.37
7.	U.S.A.			
	Washington (White)	1965	L.	1.75
	Washington (Black)		L.	1.26
8.	Libya (Jamahiriya) (Benghazi City)	1984 – 88	L.	0.28

L = Live birth S = Still Birth A = Abortion

Tabel (3): Showing pattern of cleft distribution according to the site in 20 cases*

Site	Rt.	Lt.	Bilateral	Median
Cleft palate only	1	–	–	6
Cleft lip only	–	–	–	–
Both	2	5	6	6
Total	3	5	6	6

* Description of 2 cases was not available.

Table (4) : Showing association of cleft with other congenital anomalies

Other Congenital Anomalies	No.	Percentage
Facial anomalies	10	45.45
Downs Syndrome	6	27.27
Multiple congenital anomalies	4	18.18
Piere Robin Syndrome	2	9.09
Total	2	100

Table (5) : Distribution of Cleft cases by (A) Maternal age (B) Gravida (C) Maternal blood group (D) Gestational age and (E) Birth weight.

Maternal Age in Years	No. of Cleft Cases	Percentage
20 – 25	12	45.54
26 – 30	5	27.72
31 – 35	3	13.63
36 – 40	2	9.09
Total	22	100.00

(B) : Cleft cases by maternal gravida:

Gravida	No. of Cleft	Percentage
1 – 3	9	40.90
4 – 6	8	36.36
7 – 9	2	9.09
10 – 12	3	13.63
Total	22	100.00

(C) : Cleft cases by maternal blood group:

Maternal Blood Group	No. of Cleft	Percentage
O +	5	22.72
O –	1	9.09
A +	4	18.18
A –	–	–
B +	4	18.18
B –	2	9.09
AB +	3	13.63
AB –	–	–
Not known	3	13.63
Total	22	100.00

(D) : Cleft cases according to gestation period:

Period of gestation (Weeks)	No. of Cleft	Percentage
28 – 37	6	27.27
37 – 40	15	68.18
40 +	1	4.54
Total	22	100.00

(E) : Cleft cases according to Birth Weight:

Birth Weight (gms)	No. of Cleft	Percentage
1500 – 2000	6	27.27
2001 – 2500	3	13.63
2501 – 3000	4	18.18
3001 – 3500	4	18.18
3501 – 4000	3	13.63
4001 – 4500	2	9.09
Total	22	100.00

Table (6): Showing seasonal variations of cleft:

Type of Cleft	JAN	FEB	MAR	APR	MAY	JUN	JUL	AUG	SEP	OCT	NOV	DEC
Cleft Lip Palate	–	1	–	1	1	–	–	1	–	2	3	1
Cleft Palate	–	–	–	–	–	–	–	–	2	–	–	–
Cleft&Facial Anomaly	–	2	3	2	–	–	–	–	1	–	1	1
Total	–	3	3	3	1	–	–	1	3	2	4	2
Per – Cent	–	13.6	13.6	13.6	4.5	–	–	4.5	13.6	9.09	22.7	9.09

Questionaire for Babies Born with Facial Abnormality in Jamahiriya Hospital, Benghazi. (Retrospective Study)

1 . Date and year of birth:

2 . No. of file:

3 . Type of abnormnality:

a. Facial abnormality (without cleft)

b. Cleft lip and/or palate (with or without other facial abnormality)

4 . Mother's full name:

5 . Father's full name:
6 . Residence of parents:
7 . Father's occupation:
8 . Age of mother:
9 . Blood type of mother:
10. Consanguinity 1. Yes
2. No
10. Consanguinity
11. Total number of pregnancied (G).
12. Total number of babies born full term dead or alive (P):
13. Number of still births:
14. Number of abortions:
15. Number of children alive:
16. Number of children dead:

Questions Related to Newborn:

17. Type of delivery:
18. Gestational age:
19. Sex:
20. Weight:
21. Blood type:
22. Syndrome:
23. Type of facial abnormality (not including cleft):
24. Type of cleft if present:
    1. Cleft lip:
       A. Unilateral a. Right
       b. Left
       B. Bilateral
       C. Midline
    2. Cleft palate: a. Hard
       b. Soft
    3. Combined lip and palate
    4. Cleft of uvula
    5. Cleft of alveolus
    6. Cleft a. Complete
       b. Incomplete (may be notching only)
    7. Other:
25. Write description of cleft as in file:
26. Associated body abnormalities if present:

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A Study on Activities of Intensive Care Unit of Paediatric Hospita , Tripoi (Libya)

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(Received on 5. 02 .1992)

SUMMARY

A total of 465 critically ill children were admitted to the Intensive Care Unit of Paediatric Hospital, Tripoli, from November 1990 to October 1991 . Retrospective analysis showed that among the 254 survivors (55.6%) who were discharged or transferred, respiratory infections occured in 44 children (17.32%), neurological disorders in 28 (11.02%) G.I.T. infections in 22 (8.66%) and haemopoetic diseases in 23 children (9.05%). Most of the diseases and conditions were more commonly seen in children from below 1 year to 4 years of age and gradually declined with increasing age. Females were affected by these conditions in comparison to males. The annual mortality was 211 (45.4%) and mainly during infancy 155 (73.4%). Majority of cases, 56 (26.54%), died of septicaemia and an equal number died of G.I.T. Infections (dehydration).

For further studies, a paediatric scoring system (P.S.S.) is required for comparing the activities and effectiveness of various Intensive Care Units in developing countries, and to have bettter management and outcome of critically ill children.

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الملخص

شملت هذه الدراسة (465) طفلاً يعانون من أمراض بالغة الشدة تلقوا الرعاية والعلاج بوحدة العناية الفائقة بمستشفى الجلاء الجامعي للأطفال بطرابلس خلال العام (1990 – 1991). وأوضحت النتائج أن من بين هؤلاء 254 طفلاً (55.6%) قد كتبت لهم النجاة، وبذلك رجعوا إلى بيوتهم أو حولوا إلى الأقسام المختلفة بالمستشفى، والعلل والاضطرابات التي سببت ايواءهم إلى وحدة العناية الفائقة كانت في المرتبة الأولى أمراض الجهاز التنفسي، وقد عانى منها (14.3%) من الأطفال، تلتها علل الجهاز العصبي في (11%)، ثم اضطرابات مكونات الدم في (9.1%)، فأمراض الجهاز الهضمي ومضاعفاتها وقد أصابت (8.7%) منهم، فاضطرابات الغدد الصماء في (7.5%)، والتسمم بالأدوية وخلافها ساهم في إيواء (6.3%).

وهذه العلل البالغة الشدة كانت أكثر انتشاراً بين الأطفال الذين تتراوح أعمارهم بين أقل من سنة وأربع سنوات ويتناقص معدل شيوعها بين الذين هم أكبر سناً. وبمقارنة حدوث هذه العلل بين الجنسين لوحظ أن نسبة الإناث المريضات كانت أكبر من نسبة الذكور المرضى، وكان متوسط المكوث بوحدة العناية يتراوح بين 1 – 4 أيام، وأعلى فترة مكوث كانت خمسة أيام للمعانين من علل الجهاز العصبي.

هذا وقد توفى 211 طفلاً (45.4%) خلال السنة المذكورة (90 – 1991)، وكانت أعمار 155 منهم (37.4%) أقل من السنة، وقد كان أغلبهم (26.54%) قد مات نتيجة التسمم الدموي، كما سببت اضطرابات الجهاز الهضمي (الإسهالات والتجفاف) نفس المعدل من الوفيات (26.54%)، ومن المسببات القاتلة الأخرى ذات الجنب والتهاب السحايا.

ويجدر بالذكر أن وحدة العناية الفائقة بمستشفى الأطفال بطرابلس أنشئت عام 1985م، وبها ثمان أسرة ومزودة بأجهزة الإنعاش والملاحظة المستمرة، وقد قامت بعلاج ما يربو على (1700) طفل يعانون من مختلف الأمراض الشديدة خلال الست سنوات الماضية، ويشرف عليها مستشاران في طب الأطفال ومجموعة من الأطباء المساعدين وست ممرضات مدربات خلال فترة النهار واثنتين خلال فترة الليل، وتراوحت أعمار من تلقوا العلاج بها بين أقل من سنة إلى (16) سنة، وإن كان أغلبهم أقل من (5) سنوات.

هذا ويرى الباحثون تبني الطرق التقييمية الحديثة للمقارنة بين كفاءة ونشاط وحدات الرعاية الفائقة بالدول النامية (بما في ذلك الجماهيرية) لأجل الرفع من مستوى الخدمات والعناية بأولئك الصغار الذين هم بين الموت والحياة.

INTRODUCTION:

Critical illness is common in both adults and children, in developing countries. However, intensive care paediatric units lack skilled manpower, require better facilities, and have a heavy work load, and economical difficulties. Poor use of health services available to the community, and poor health education lead to delayed recognition of seriously sick children.

The cost – effectiveness of intensive care units has been examined in Western countries (1 – 4), but there has been no such reports from the developing world.

The present study was undertaken to assess the effectiveness and value of intensive unit in providing emergency care to children with a wide range of paediatric problems in different age group

PATIENTS AND METHODS:

The intensive care unit of the Teaching Paediatric Hospital, in Tripoli (Libya) was established in Nov. 1985 . Until October 1991 , over 1700 patients were admitted and managed for various clinical conditions. Age ranged from birth to 16 years.

It is an 8 – bedded unit, with an average bed occuphncy of 8 patients per day. There is one registrar, 4 residents, and two consultants who we al have full time commitments. Eight trained nurses work in the unit by day. At night, it is covered by the on – call paediatricians.

The unit has 3 ventilators, one defibrillator, and 8 vital – signs – monitors. Endotracheal tubes, humidifiers, blood gas machine, and portable X – ray are also available.

The present study included 465 children who were admitted directly or referred from other hospitals and treated in the intensive paediatric care unit during the period from Nov. 1990 to Oct. 1991 . Information and data were collected and analysed from their case records according to age, sex and type of emergency. Emergency surgery and accident cases are not included, since these cases are admitted to the Trauma department of Tripoli hospital.

All patients considered by the doctor to need intensive care were admitted and were later discharged or transferred back to their respective unit for furter management and follow – up.

RESULTS

Of the 465 children studied, 235 (50.5%) were males and 230 (49.5%) females. Their ages varied from below one year to sixteen years (Table 1).

Two hundred and fifty four (556%) of these children survived and were discharged/transferred from. I.C.U. respiratory diseases accounted for 44 cases (17.32%), and central nervous system diseases for 28 cases (11.02) and were the most common paediatric problems among children upto 4 years of age (Table 2).

Table 3 shows that respiratory, C.N.S., endocrinal and diseases, were higher in females than males, whereas cardiovascular diseases, G.I.T., nutritional diseases and drug poisoning were more common in males. However for haemopoetic diseases, the sex ratio was similar.

The total annual mortality among all children was 211 (45.4%). Mortality in children below 1 year and 1 – 4 years was higher in comparison to that of other age groups (Table 4). Septicaemia and dehydration, followed by meningitis and pneumonia, were the major killers in these children.

The duration of stay in I.C.U. varied from 1 – 5 days for the various conditions (Table 5), but C.N.S. cases stayed longest (medium 5 days).

DISCUSSION

The results of the present study showed that respiratory, central nervous, haemopoetic and G.I.T. infections were more common during the first four years of life, and declined with increasing age. The major morbidity conditions diagnosed were pneumonia, bronchial asthma, diarrhoea, dehydration, septicaemia, meningitis, epilepsy and, to some extent, congenital abnormalities. A similar study was conducted in Northampton (7) where, excluding road accidents and surgical emergencies, respiratory infections

were commonest in children aged 12 years and under, who were admitted in the intensive therapy unit.

Respiratory, C.N.S., G.I.T. and endocrinal diseases occurred more in female than male children. However, no reason for the sex difference for these particular diseases have been found (12) although it is known that most of the respiratory and G.I.T. infections are commonly affected by season (9).

Septicaemia was also common, and the etiological pathogen responsible for most cases was klebsiella. This is in contrast to previous studies which reported betahaemolytic stretococci belonging to Group A or B as the predominantly isolated organisms in neonatal septicaemia (3, 6).

Higher mortality was seen among children upto 4 years of age, which reflects higher vulnerability of children of preschool age. Septicaemia dehydration, meningitis, epilepsy and pneumonia were the commonest cause of death in this age group This is similar to others reports from Tripoli (2, 1), where septicaemia was one of the main causes of infant death and accounted for 167 and 123/100,000 live births during the year 1988 and 1989 in Libya.

Deaths due to G.I.T. infection (diarrhoea, dehydration) could only be explained on the basis of the associated risk factors to which the child was exposed before being admitted to the unit. These risk factors can be overcrowding, infected food, poor personnel hygiene, and environmental sanitary conditions. Artificial, rather than breast – feeding, may also be an important factor.

The figures from this I.C.U. show that a wide variety of acute illnesses have been looked after in the unit with participation of full – time medical staff.

The majority of morbidity mortality conditions occurred from birth to 4 years of age. Respiratory infections were highest among all the infections, where as the mortality pattern showed that most of the children died of septicaemia, followed by C.N.S. and respiratory ingections. Further, this mortality was higher in females than males. There was no mortality from drug poisoning and endocrinal diseases.

In the present situation, with limited resources of emergency care personnel, as well as equipment, and limited services from the laboratories, it is suggested that certain carefully selected child patients do benefit from intensive therapy units and for this reason deficient paediatric ICUs in developing countries should be well designed, and fully equipped and staffed.

A staff of highly trained nurses authorised to take immediate action in emergency situations must be available 24 hours. Managing an intensive care unit today goes well beyond a single physician's or nurse's capabilities – it requires team work (11).

There is still a need for a comprehensive yet simple pediatric scoring system for comparing the efficacy and outcome of paediatric intensive care in different ICUs in different countries. Two scoring systems have been specifically developed for infants and children in intensive care in the U.S.A. They are the physiologic stability Index (PSI) (15) and the organ system failure (OSF score) (14) and they are ready for international use (13) .

Although the study has highlighted the major paediatric problems, a scoring system must be more widely used in the description and prediction of the outcome of children undergoing intensive care.

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Tabel (1): Distribution of Cases According to Age and Sex

Age (Years)	Maele (n = 235)		Female (n = 230)		Total (n – 465)	
	No.	(%)	No.	(%)	No.	(%)
1	136	(57.8)	139	(60.4)	275	(59.1)
> 1 to 4	46	(19.5)	43	(18.7)	89	(19.1)
> 5 to 8	23	(10.0)	18	(8.0)	41	(8.8)
> 9 to 12	20	(8.5)	20	(8.6)	40	(8.6)
> 13 to 16	10	(4.2)	10	(4.3)	20	(4.3)

Table (2) : Common morbidity conditions among discharged/ transferred cases from I.C.U. According to their various age groups.

Morbidity Conditions	Age in years					
	1 No. (%)	1 – 4 No. (%)	5 – 8 No. (%)	9 – 12 No. (%)	13 – 16 No. (%)	Total No. (%)
Respiratory Diseases	20 (20.00)	12 (20.30)	1 (3.30)	7 (23.30)	– –	44 (17.32)
C.M.S. Diseases	12 (10.00)	4 (06.50)	3 (10.00)	6 (20.00)	3 (20.00)	28 (11.02)
Haemopoetic Diseases	14 (11.70)	5 (08.50)	1 (3.30)	– –	3 (20.00)	23 (9.05)
G.I.T. Diseases	15 (12.50)	3 (05.10)	3 (10.00)	– –	1 (6.70)	22 (8.66)
Endocrinal Diseases	1 (00.80)	3 (05.10)	6 (20.00)	8 (26.70)	1 (06.70)	19 (07.48)
Renal Diseases	1 (00.80)	– –	1 (03.30)	2 (06.70)	2 (13.30)	6 (02.36)
C.V.S. Diseases	3 (02.50)	4 (06.80)	1 (03.30)	1 (03.30)	2 (13.30)	11 (04.33)
Nutritional Diseases	3 (02.50)	2 (03.40)	– –	– –	– –	5 (01.96)
Drug* Poisoning	–	14 (23.70)	2 (06.70)	–	–	16 (06.29)
Others**	47 (39.20)	12 (20.30)	12 (40.00)	6 (20.00)	3 (20.00)	80 (31.49)
Total	120	59	30	30	15	254

N.B.: Figures in brackets indicate percentage.

* Paracetamol, insecticidal and kerosine poisoning were more commonly seen in 1 – 4 year age group children. In 5 – 8 year age group children only paracetamol poisoning was seen.

** Congenital abnormality excluding congenital heart disease was found in < 1 and 1 – 4 year age groups. Werdning syndrome was also found < 1 year of age. Whereas Sturge – Weber syndrome and few cases of drowning, scorpion bite, systemic lupus erythematosus were present in 1 – 4 year age group. Septic shock, scorpion bite, septic arthritis in 5 – 8 years of age. Same conditions like septic shock and arthritis were seen in 9 – 12 and 13 – 16 years of age group children.

Table (3): Sex ratio in relation to various systems involved in diseases of children in I.C.U.

Systems	Sex Ratio		
	M	%	F
– Respiratory	1	:	1.03
– C.N.S.	1	:	1.40
– C.V.S.	1	:	0.90
– Haemopoeitic	1	:	1.00
– G.I.T.	1	:	2.10
– Nutritional	1	:	0.00
– Endocrinal	1	:	1.50
– Drug Poisoning	1	:	0.70
– Others	1	:	0.20

Table (4) : Causes of death among I.C.U. cases according to their various age groups

Causes of Death	Age in Years					
	1 (n = 155)	1 – 4 (n = 30)	5 – 8 (n = 11)	9 – 12 (n = 10)	13 – 16 (n = 5)	Total (n = 211)
Respiratory Diseases	11 (7.0%)	4 (13.3%)	2 (18.2%)	1 (10.0%)	– –	18 (8.53%)
Haemopoetic Diseases	45 (29.0%)	4 (13.3%)	3 (27.3%)	2 (20.0%)	2 (40.0%)	56 (26.54%)
G.I.T Diseases	48 (31.0%)	3 (10.0%)	2 (18.2%)	2 (20.0%)	1 (20.0%)	56 (26.54%)
C.N.S. Diseases	9 (05.8%)	8 (26.7%)	3 (27.3%)	1 (10.0%)	1 (20.0%)	22 (10.43%)
Endocrinal Diseases	–	–	–	–	–	–
Renal Diseases	2 (1.2%)	1 (3.3%)	1 (9.0%)	–	–	4 (1.89%)
C.V.S. Diseases	6 (3.8%)	–	–	–	–	6 (2.85%)
Nutritional Diseases	2 (1.2%)	1 (3.3%)	–	–	–	3 (1.42%)
Drug Poisoning	–	–	–	–	–	–
Others	32 (21.0%)	9 (30.0%)	–	4 (40.0%)	1 (20.0%)	46 (21.80%)

Table (5): Distribution of cases according to their median duration of stay.

Type of Cases	Median duration of stay Days
C. N. S. Cases	5
Respiratory Cases	4
C. V. S. Cases	4
Haemopoetic Cases	4
G. I. T. Cases	3
Renal Cases	3
Endocrinal Cases	3
Drug Poisoning Cases	1

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Guillian Barre' Syndrome in Libya

(A Review of 25 Cases)

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(Received on 21 .1993)

SUMMARY

We present a clinical review of 25 patients of Guillian Barre ' Syndrome admitted to Al – Fateh Children Hospital, Benghazi, over period of 4 years. The majority of cases were seen in the year 1990 . There were no significant seasonal variations, M:F, 1:1.5, age range 9 months – 13 years, mean age 4 years. Their presentation, course of recovery and outcome were studied. Nine patients received steroids, 16 did not. Twenty children recovered completely. Six patients required ventilation. Three died. Two patients were left with permanent neurological sequelae. The need for the use of new modalities of treatment, such as I/V Immunoglobulins, or Plasmapheresis, specially in those patients who show factors predicting for poor outcome, is stressed.

الملخص

في هذه الدراسة نتطرق لعدد من حالات متلازمة غليان باري في الأطفال (25 حالة) تم علاجهم بمستشفى الفاتح لطب وجراحة الأطفال خلال 4 سنوات، معظم الحالات شخصت عام 1995م، ولم يكن هناك تأثير مناخي يذكر خلال هذا العام. وكانت نسبة الذكور إلى الإناث 1: 1.5 ، وكان معدل العمر 4 سنوات.

وقد تمت دراسة أعراض المرض وتطوره ونتائج العلاج: 9 أطفال عولجوا بالستيروئيد و16 طفلاً لم يعالجوا بالستيروئيد، 20 طفلاً تم شفاؤهم بالكامل، و6 أطفال احتاجوا إلى استخدام الجهاز التنفسي الصناعي.

ثلاث أطفال توفوا، وطفلان أصيبوا بإعاقة عصبية مزمنة، كما تناقض الدراسة أهمية وجود التقنية الجديدة لعلاج هذا المرض ووجوب توفرها في بلادنا.

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INTRODUCTION

Guillian Barre' Syndrome, or acute inflammatory demyelinating polyradiculoneuropathy (AIDP), is an autoimmune disorder which requires both an altered immunological response and an extrinsic triggering factor. The trigger in childhood is usually a viral or mycobacterial infection. The first symptom is weakness which has an acute onset progressing for few days, remaining stationary for few weeks, followed by recovery over several months (13). In the acute state supportive treatment, assisted respiration and tracheostomy may be necessary. The value of treatment with steroids has been debated.

Generally the prognosis is good, most children recover with mild or no sequelae. Death may be due to respiratory complications during the acute phase, and occasiomally patients survive with severe permanent neurological weakness.

This paper describes the clinical features, natural course of G.B. Syndrome in patients from Eastern Libya.

PATIENTS AND METHODS

This study was done in El – Fateh Children Hospital, a major referral university hospital in the Eastern part of Libya serving about 1.5 million population, of whom more than 50% are less than 13 years of age. 25 children (15 females and 10 males), age range 9 months – 13 years, were admitted in the period between January 1987 to December 1990 and identified clinically as having acute Guillian Barre' Syndrome. The diagnosis was based on Osler and Sidel (1960) criteria (9); onset after an infection; early sensory symptoms with minimal objective sensory findings; progressive; symmetrical weakness; reduced or absent deep tendon reflexes; elevated C.S.F. protein level with no increase in cell count; and an eventual marked improvement. Their clinical details included symptoms and signs, preceding illness, time of appearance and improvement, and time of full recovery, C.S.F. results for all patients at the time of admission. Complications and outcome were also recorded. Only 9 children (36%) received prednisolone orally in a dose of 2 mg/kg/day in 3 – 4 divided doses for 2 weeks and tapered over another week, plus supportive respiratory treatment when needed and regular physiotherapy. The other 16 children (64%) received supportive respiratory treatment when needed and regular physiotherapy. During their stay in hospital, patients were examined daily for signs of clinical improvement. Those children who showed improvement in their muscle power within 3 weeks of onset of the disease were considered as early improvers, while those who showed clinical improvement after 3 weeks as late improvers. After discharge, they were regularly followed up by one of us for a period of 1 – 3 years. After 1 year follow up, those children who had muscle power of 3 or less (MRC Scale) were considered as having a permanent neurological sequelae.

RESULTS

Out of the 25 cases of G.B. Syndrome (15 were girls and 10 were boys) (M/F 1.5 :1), (mean age 4 years) 13 children (52%) were under 4 years of age, and 22 children (88%) were under 6 years of age. Only one child was below one year of age, and other 3 children were between 10 – 13 years.

Sixteen children (64%) were seen during 1990 , but, during this year, there were no significant seasonal variations.

A viral URTI was the preceding illness in 20 children (80%); but no antecedent illness was noted in the other 5 children (20%).

All children were admitted with an acute ascending paralysis of lower motor neurons type. Six children (24%) had a very rapid course, with respiratory muscle involvement within 24 hours of admission, and all required artificial respiration. Three of them died at this stage, 2 were ventilated for 2 weeks followed by tracheostomy for more than 6 months, and had a permanent neurological sequelae.

Nineteen children (76%) had a rather mild course without involvement of respiratory of respiratory muscles. Ten children (40%) had sensory symptoms in forms of pain and tingling. Autonomic nervous system disturbance, bladder

involvement and arrythmias were recorded in 5 children (20%).

Eight children (32%) had cranial nerve involvement, as follows: 1 child had isolated bulbar involvement; 6 children had both 7th nerve and bulbar involvement, 1 child had unilateral 6th nerve involvement. The last child had pseudotumour cerebri (Table 1). Regarding the CSF results of all children on admission, only 3 children had more 10 lymphocytes/c.c in their C.S.F., the others had no cellular reaction. Thirteen children (52%) showed elevated C.S.F. protein levels 45 mg/dl, while 12 children (48%) showed normal C.S.F. protein levels.

One week after admission, CSF reanalysis in these 12 children showed protein levels of more than 45mg/dl in 9 children (36%) while it remained normal in 3 children (12%). Time of appearance of recovery was recorded in 18 children only, 10 children (56%) showed signs of recovery within 3 weeks of onset and 8 children (44%) showed signs of recovery after 3 weeks. Three children (12% of total) died during first week of illness, 2 of them received steroids, and all of them required artificial ventilation and antibodies for secondary respiratory infection. Two children (8% of total) had permanent neurological sequelae; on of them received steroid and one didn't. One child (4% total) had a relapse within one year. Twenty children fully recovered (80%). In the poor outcome group (died or had permanent neurological sequelae) all 5 children (100%) had a very rapid progressive course with established paralysis within a week; 3 children (60%) were below 1.5 years of age; 4 children (80%) required artificial ventilation. In the good outcome group of 20 children; 8 (40%) had a rapid progressive course; 2 (10%) were below 1.5 years of age and 2 (10%) required artificial ventilation (Table 2).

DISCUSSION

The calculated annual incidence of Guillian Barre' syndrome in Libyan children is approximately 1/100,000 per year, while the incidence elsewhere has varied from as low as 0.38/100.000 in Finland (10) to an adjusted incidence of 1.8/100,000 per year in American children (2). Guillian Barre' Syndrome remains a serious condition, and in our series, three out of 25 cases (12%) died and two (8%) were left with permanent sequelae.

Briscoe et al (1) reported 4% mortality and 12% of his series were left with neurological sequelae. While J.C. Raphael (11) had mortality of 10% and 405 were left with permanent neurological sequelae. However his study included both adults and children (age range 2 – 81 years; mean age 40.6 years). Recently Rantala et al in Finland reported to deaths and only one child out of 27 cases (3%) had permanent neurological sequelae (10). The role of steroids is controversal, and they are no longer recommended by some workers (9,7). Poor prognostic features in our study included rapid progressive course, need for ventilation assistance, and younger age. These criteria could be useful in deciding the need for early therapeutic intervention with new modalities of treatment like plasmapheresis, and recently high dose I.V. immunoglobulins. There is a real need for considering the use of these recent management approaches on out – patients in Libya and also to evaluate their usefulness by proper prospoective studies (8,6,4,13,5).

Table (1) : Clinical Features

Clinical Features	No. of Patients (%)	
ASCENDING PARALYSIS	25	(100%)
i) Rapidly Progressive course	4	(25%)
ii) Slowly progressive course	19	(76%)
SENSORY SYMPTOMS AS PAIN AND TINGLING	10	(40%)
MENINGEAL IRRITATION	4	(16%)
AUTONOMIC NERVOUS SYSTEM DYSFUNCTION	5	(20%)
CRANIAL NERVES INVOLVEMENT	8	(32%)
i) Bulbar involvement	1	(4%)
ii) 7th nerve and bulbar	6	(24%)
iii) 6th nerve	1	(4%)
PAPILLOEDEMA	1	(4%)

Table (2) : Significance of Poor Prognostic Factors.

	Poor Outcome (5 Children)*		Good Outcome (20 Children)		P Value
	No.	(%)	No	(%)	
i. AGE 1.5 years	3	(60%)	2	(10%)	0.05
ii. Rapid progressive course (Peak deficit week)	5	(100%)	8	(40%)	0.01
iii. Ventilatory Assistance	4	(80%)	2	(10%)	0.01
iv. Time of improvement 1 month	2	(40%)	10	(50%)	0.5
v. C.S.F. cells 10/c.c.	0	(0)	2	(10%)	0.1
vi. Presence of bulbar involvement	2	(40%)	5	(25%)	0.25

* (13 Death, 2 Permanent Sequale).

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The Hypocholesterolemic Effect of Chloroquine in Rat

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SUMMARY

Female rats were injected with Chloroquine at dose of 10 mg/Kg/ day for ten days. The drug caused a significant reduction in the total serum cholesterol and phospholipids by 25% and 55%, respectively. Both HDL – chlesterol and VLDL + LDL – cholesterol fractions were lowered proportionally without altering the percentages from total cholesterol. On the other hand, neither the hepatic cholesterol nor the phospholipid contents were affected by the chloroquine treatment. The drug significantly depressed the ratio of esterified cholesterol: free cholesterol in both serum and liver tissue.

الملخص

تم حقن إناث الفئران بعقار الكلوروكوين بجرعة قدرها عشرة مليجرامات لكل كيلوجرام من وزن الجسم ولمدة عشرة أيام متتالية. اتضح من النتائج أن عقار الكلوروكوين أدى إلى نقص ذي دلالة احصائية في مستوى الكلسترول الكلي في المصل وكذلك الفسفوليبيدات. كذلك أوضحت النتائج أن البروتينات الدهنية عالية الكثافة، والمنخفضة، والمنخفضة جداً، قد انخفضت دون تأثير على نسبها من الكلسترول والفوسفوليبيدات في الكبد. بحساب النسبة بين الكلسترول استر، والكلسترول في المصل والكبد، اتضح بأن العقار أدى إلى انخفاض ذي دلالة احصائية بهما.

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INTRODUCTION:

Chloroquin (CQ) is a lysosomotropic amine which accumulates in the lysosomes and disrupts the normal functions of the lysosomal enzymes (5). The drug is known to inhibit the lysosomal degradation of phospholipids (13), and impair the catabolism of low density lipoprotein (LDL) in cultured fibroblasts, without affecting its uptake by the cells (7). CQ has also been reported to inhibit the biosynthesis of cholesterol in the isolated rat liver (3). Most of the reports investigating the influence of CQ on cholesterol mobilization have been carried out in isolated cell cultures, and since as high as 70% of the body cholesterol is believed to be derived from de novo synthesis (4), therefore, this study was planned to investigate the effects of CQ on the homeostasis of cholesterol and phospholipids in the rat.

MATERIALS AND METHODS:

Twenty adult female Sprague Dawley rats weighing between 200 – 250g were used in this study. The animals were divided randomly into two groups and housed in plastic cages at room temperature of 24±◦ C and relative humidity 50 – 60%. The experimental group was injected intramusucularly (i.m.) with 10 mg/kg/day of chloroquine prepared by dilution of chloroquine phosphate in physiological saline, and given daily in two divided doses in physiological saline, for ten consecutive days. The control group received similar volumes of physiological saline. The rats had free access to a nutritionally adequate pelleted diet (Public Company for Animal Feed Production, Benghazi, Libya) and tap water. After the last injection the animals were fasted overnight and sacrificed by decapitation. Blood collected from trunk and serum was separated by centrifugation. Liver was dissected rapidly, washed in cold saline and kept frozen (70 C) for a maximum of four days awaiting analysis. The total Lipids of aliquots from serum, or weighed portions of liver, were extracted with chloroform – methanol 2 :1 (v/v), centrifuged and the solvent was evaporated under a stream of nitrogen.

The total cholesterol was estimated enzymatically by the method of Allain et al (1). The total phospholipids (PL) were determined as total phosphorus by the method described by Bartlett(2), and choline phospholipid concentration by the enzymatic method of Takayama et al (14). The high density lipoprotein (HDL) – cholesterol was determined after precipitation of the Apo B – containing lipoproteins with heparin and manganese chloride as described by Lopes – Virella (9). The combined cholesterol fractions of very low density lipoprotein (VLDL) and LDL was calculated by subtraction of the HDL – cholesterol from total plasma cholesterol. The ratio of esterified to free cholesterol (EC/FC) was determined following separation of the cholesterol fractions on thin layer chromatography plates using Silica gel G as described previously (8).

Statistical Analysis:

Results are expressed as means + S.E.M. The significance of differences between the experimental and control groups were evaluated by the Student's 't' test of unpaired data. P values less than 0.05 were considered significant.

RESULTS:

Rats treated with CQ (10mg/kg/day) for ten days showed significant reduction in serum total cholesterol, which amounted to 25% less of that of control (Table 1). Both HDL and the combined LDL and VLDL cholesterol fractions were significantly lowered at a similar rate leaving the final percentages of HDL and LDL + VLDL from total cholesterol unchanged (71.5% and 28.4%, respectively).

The CQ treatment lowered the serum esterified cholesterol by 14.3%, as shown by the reduction in the ratio of esterified to free cholesterol.

A reduction of 55% in the total serum PL was also discernible following the drug administration. The Choline – phos – pholipid fraction of total PL was significantly raised.

Neither the total cholesterol nor the PL content of liver were altered by CQ treatment (Table 2).

Table (1) : Effect of chloroquine (10mg/kg/day) or physiological saline administered intramuscularly for 10 consecutive days on serum cholesterol and phospholipids

Parameter	Control	Chloroquine Treated
Total Cholesterol (mmol/1)	1.36 ± 0.076	1.02 ± 0.046*
HDL – Cholesterol (mmol/1)	1.01 ± 0.062	0.73 ± 0.03 *
VLDL + LDL – Cholesterol (mmol/1)	0.35 ± 0.006	0.29 ± 0.007*
Esterified Cholesterol /Free Cholesterol Ratio	2.23 ± 0.026	1.91 ± 0.048**
Total Phospholipids (mmol/1)	9.59 ± 0.198	4.29 ± 0.066***
Choline Phospholipids(mmol/1)	1.53 ± 0.048	1.01 ± 0.038***
% Choline Phospholipids From Total Phospoholipids	15.97 ± 0.50	23.44 ± 0.89***

Values represent Means ± S.E.M. (n = 8) Statistical analysis by Student's 't' test for unpaired values
*P< 0.05 . ***P< 0.001.

Table (2): Contents of cholesterol and phospholipids in the rat liver following treatment with chloroquine (10mg/kg/day) or physiological saline (control) administered intramuscularly for ten consecutive days

Parameter	Cotrol	Chloroquine treated
Total Cholesterol (umol/g tissue)	35.76 + 0.66	36.27 + 1.51
Esterified Cholesterol/ Free Cholesterol Ratio	0.29 + 0.01	0.22 + 0.01*
Total Phospholipids (umol/g tissue)	23.80 + 0.49	23.30 + 0.51
Choline – Phospholipide (umol/g tissue)	9.39 + 0.23	8.22 + 0.23*
% Choline Phospholipid From Total Phospholipids	39.45 + 0.96	35.31 + 1.01*

Values represent Means± S.E.M. (n = 8). Statistical analysis by Student's 't' test for unpaired values, *P< 0.05 .

However, the content of choline – phospholipid as well as its percentage from total hepatic PL were significantly reduced. The esterified fraction of hepatic cholesterol was also significantly reduced (– 24%) following the drug treatment.

DISCUSSION:

Results of the present study have demonstrated that the treatment of normolipidemic rats with CQ (10mg/kg/day) for ten days caused a significant reduction in the serum total cholesterol. The treated animals did not show any loss of body weight or liver weights (results not shown) following the CQ treatment, which indicates that the drug had no effect on the feed intake. The results are consistent with the findings of Beynen et al (3), who reported that CQ was a potent inhibitor for cholesterol biosynthesis, but not the fatty acid synthesis, in the isolated rat liver. The inhibitory action of the drug was, therefore, suggested to be on the biosynthetic pathway of cholesterol beyond the cytosolic acetyl CoA

branch point of cholesterol and fatty acid synthesis. Several reports have also shown that CQ inhibited the secretion of VLDL from cultured rat hepatocytes (12, 10). The inhibition of lipoprotein release was found to be associated with swollen Golgi cristernae which contained VLDL – like particles (12). The inhibition was attributed to CQ, being a cationic amphiphilic drug, tends to accumulated to CQ, being a cationic amphiphilic drug, tends to accumulate in the acidic Golgi vesicles and disturb the intracellular proton gradient which in turn disrupts the flow of lipoprotein across the membrane (10). In our study, the 17% reduction in the amount of cholesterol associated with VLDL and LDL was compatible with the idea that CQ may have impaired the release of VLDL into circulation. A noteworthy finding in the present study was the significant reduction (28% of that of control) in the HDL – colesterol. However, the risk factor calculated as the ratio of HDL – cholesterol/total cholesterol, remained unchanged. Moreover, the present results have shown a reduction in the ratio of esterified cholesterol to the free cholesterol following the drug treatment. Explanation of the mechanism underlying this change, however, must await further investigations. Some investigators have shown that CQ inhibited the proteolytic degradation of LDL in human fibroblasts (7) and suppressed the catabolism of chylomicron remnants in cultured hepatocytes leading to the accumulation of lipoprotein remnants in the cells (6). In contrast, the present results did not show any increase in the hepatic lipid contents. A possible explanation to this controversy is that, thus far studies reported in the literature were performed in isolated cells and the organ interaction is lacking, secondly, CQ is known to enhance the secretion of cholesterol into bile (11), which may have contributed to the disposal of cholesterol from liver preventing its accumulation in the tissue.

It is premature, however, to give a conclusion about the clinical usefulness of CQ in the treatment of hypercholesterolemia but, never the less, the present report suggests that chloroquine may form the basis of a new class of hypocholesterolemic drugs, pending further investigations.

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Thyroid Carcinoma - A Study of 83 Cases from Eastern Libya

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SUMMARY

Thyroid carcinoma is relatively uncommon with varying geographic incidence. We could collect 83 cases over a span of twelve years and our analysis provide that the frequency of thyroid acrcinoma is low in Eastern Libya. It also confirmed the female predominance, common occurrence around the fourth decade of life, and that papillary carcinoma was the most common histological type.

الملخص

يعتبر مرض سرطانة الغدة الدرقية من الأمراض الغير شائعة نسبياً، وهي ترتبط بمناطق جغرافية من ناحية انتشارها. فخلال فترة اثنتا عشرة سنة تمكن القسم من تشخيص حوالي ثلاث وثمانون حالة فقط من مجموع حوالى 520 حالة مرضية بالغدة الدرقية في المنطقة الشرقية من الجماهيرية. وقد بين التحليل الاحصائي أن سرطانة الغدة الدرقية بهذه المنطقة غير شائع، ثم إن معظم المرضى من الإناث في سن الاربعينيات، وأن أكثر الأنواع انتشاراً هو السرطانة الحُليمية (Papillary Carcinoma).

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INTRODUCTION:

Clinically apparent thyroid carcinoma is relatively uncommon. The reported annual incidence ranges from 0.3 to 10 per 100,000 persons (13,14). There is great variation in the incidence figures throughout the world, with the highest reported rates of clinically detected thyroid cancer from Iceland, Israel and Hawaii, and low frequency rates from Britain, Romania and Hungary (8). There is a definite prevalence of thyroid cancer in females as compared to males (10). The prognosis of thyroid cancer is in general worse in endemic goitrous countries than in goitre – free areas. We have studied 83 cases ot thyroid carcinoma based on surgical pathology material available over a period of twelve years.

MATERIALS AND METHODS

There is no existing cancer registry in Libya and there are no post – mortems done. Therefore our analysis is mainly from the material available from the histopathology records maintained by the department of pathology, Al – Arab Medical University, Benghazi. Our department is the referral centre for histopathology for the entire Eastern Libya. Thyroid neoplasma reported between January 1981 and December 1992 were collected and analyzed according to age, sex and histological type. Histopathology slides were available for all these cases, and whenever necessary, new sections were cut and special stains were used. These cases were classified histologically based on World Health Organization (WHO) histological classification on thyroid tumours(5).

RESULTS

The total number of biopsies received by the department during the study period was 69,352, out of which 4251 were malignant lesions in general, and 83 were thyroid neoplasms. The frequency of thyroid carcinomas is found to be 0.1 percent. Papillary carcinoma was the most common histological type (59%) followed by follicular carcinoma (27.7%) (Table 1). Females were more commonly affected than males; the malefemale ratio was 1:3.15 . Third and fourth decades were found to be the most common age range for thyroid carcinomas (Table II). Sarcomas or other malignant tumours (non – epithelial) were not observed in the present study.

DISCUSSION

There is great geographic variation in the incidence of thyroid malignancies. Initially this variation was attributed to endemicity of goitre in high fequency regions. But the recent data suggest that there is no correlation between the incidence of thyroid cancer and endemic goitre (5). Goitre is not an endemic health problem in Eastern Libya. This is obvious from our material where there were only 932 thyroidectomies out of a total number of 69, 352 biopsies between 1981 and 1992. The frequency of thyroid carcinoma appears to be low in our study. Our data also suggests that possibly there is no relation between thyroid cancer incidence and endemicity of goitre.

Clinically apparent thyroid carcinoma is more common among females, on average one male is affected for every three females. The sex difference is particularly marked in papillary and follicular carcinomas, but is much less so in medullary and undifferentiated carcinoma (15). Similar observations were in our study also. Interestingly the marked female preponderance seen in clinical thyroid carcinoma is not present in studies of the prevalence of occult thyroid carcinoma (1, 12). This preponderance completely disappears and even reverses, if the examination of the thyroid provides an adequate histopathological representation of the smallest tumor. In the present study the number of cases of occult carcinomas (4) were too few to make a sensible analysis. The absence of post – mortem study of all hospital deaths in this country deprives the diagnosis of occult carcinoma in general. The reason for larger thyroid carcinomas in females than in males is not known. The presence of a promoting (?Hormonal) factor in females which is lacking in males has been suggested as a possible explanation (11).

Thyroid carcinoma is rare in childhood (2). Currently it has been estimated that about 10% of all thyroid carcinomas occur in patients under 21 years of age (3). In the present study also the peak incidence of thyroid cancer was observed above the fourth decade.

The prognosis of thyroid cancer is generally worse in regions with endemic goitre. This can be explained by two important factors:

a) Thyroid cancer patients in endemic goitre areas are first seen only in advanced tumor stage, as 'Lump in the neck' is considered a normal development in these areas.

b) In general, highly aggressive histological tumor types are present in a large part of thyroid cancer areas from endemic goitre areas. While prognostically more favourable tumors prevail in goitre free countries (10). Unfortunately we cannot comment on prognosis aspect in our study as there is no follow up.

Papillary Carcinoma:

Papillary carcinoma is the most common form of differentiated thyroid carcinoma accounting for 60 – 70% of all thyroid carcinomas in most series (8). Clinically it is diagnosed two to four times more often among females than in males and it may occur at any age, the mean age being 40 years. In the present series also it is the most common type accounting for 59% of all thyroid carcinomas. Females were nore frequently affected than males (MF ratio 1 :5). The most common age of presentation was 3rd and 4th decades.

Follicular Carcinoma:

Follicular carcinoma is the second most common type of thyroid carcinoma accounting for 10 – 30% of thyroid carcinomas in most series (8). The marked variation in incidence reported in different series may be due partially to geographic variation and environmental factors. There is some evidence that follicular carcinoma is more common in endemic goitre areas (4). Follicular carcinoma has a similar predilection for females as papillary carcinoma. The average age at diagnosis ranges between 48 years (6, 15). In the present study follicular carcinoma accounted for 27.7% of all thyroid carcinoma. It was more common in females (MF ratio 1:2.2) and fifth decade was the most common age at presentation.

Medullary Carcinoma:

Medullary carcinoma accounts for 4 – 12% of all cases of thyroid carcinoma. Sporadic medullary carcinoma usually presents in middle age (45 – 55 yrs) whereas as symptomatic cases of the familial form most often become apparent a decade earlier. In most series a slight female preponderance is noted (7). In the present study medullary carcinoma accounts for 4.8% of all cases of thyroid carcinomas. All cases were sporadic cases except one which occured in 19 year old girl.

Anaplastic Carcinoma:

Also referred as undifferentiated thyroid carcinoma, may be defined as a neoplasm composed in part or exclusively undifferentiated cells. It belongs to the most aggressive malignat tumors occurring in humans. It accounts for approximately 5 – 10% of all thyroid carcinomas and mainly presents in the elderly (5,9). Most cases occur in the seventh and eighth decades of life with a slight female preponderance. In the present study it accounted for 8.4% of all thyroid carcinomas and seventh and eighth decades were the most common age at presentation with a slight female preponderance (MF ratio 1 :1.3).

There were no cases of non – epithelial malignant tumors in the present study.

Table (1) : Shows incidence of various histological types of thyroid carcinoma in males and females.

Histological Type	Total	Male	Female	M:F Ratio	Percent
Papillary Carcinoma	49	8	41	1: 5.1	29
Follicular Carcinoma	23	7	16	1: 2.2	27.7
Medullary Carcinoma	4	2	2	1: 1	4.8
Anaplastic Carcinoma	7	3	4	1: 1.3	8.5
Total	83	20	63	1: 3.15	100

Table (2) : Age incidence of various histological types of thyroid carcinoma

Histological Type	0 – 20 yrs	21 – 30 yrs.	31 – 40 yrs.	41 – 50 yrs.	51 – 60 yrs.	61 – 70 yrs.	70 and above	Total
Papillary Carcinoma	2	12	15	11	5	4	–	49
Follicular Carcinoma	2	4	5	6	2	2	2	23
Medullary Carcinoma	1	–	–	1	–	2	–	4
Anaplastic Carcinoma	–	–	1	1	–	3	2	7
Total	5	16	21	19	7	11	4	83

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The Pattern of Thyroid Disease in North - Eastern Libya

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SUMMARY

An 11 – year retrospective survey of 706 Thyroidectomy specimens in North – Eastern of part of Libya shows that there were 602 females and 104 males giving a sex ratio of 6 :1. 49.5% had simple goitre, 25.2% had adenoma, 10.33% had carcimona, 5.8% had Grave's disease, 4.5% had various types of thyroiditis. Simple goitre is the commonest cause of thyroid swelling. Incidence of thyroid carcinoma is higher than that reported from Europe and U.S.A.

الملخص

تقدم هذه الدراسة التي تعود إلى أحد عشر عاماً سابقة وما بعدها، نتائج استقصاء (706) عينات من الغدد الدرقية المستأصلة من مرضى في منطقة شمال شرق ليبيا، كان من بينها (602) عينة تخص الإناث و(104) عينة تخص الذكور (أي بنسبة إناث: ذكور 1:6).

أظهرت هذه العينات بعد الفحص أن نسبة (49.5%) منها كان بسبب الدراق البسيط، و(25.2%) منها تورم غدّي، و(10.33%) تورم سرطاني، و(5.8%) منها مرض غريفز، و(4.5%) منها التهابات درقية متنوعة. ونرى أن الدراق البسيط هو أهم أسباب تورم الغدة الدرقية..

كما أن نسبة حدوث سرطان الدرقية في هذه المنطقة أعلى من النسب المسجلة في أوروبا والولايات المتحدة الأميركية.

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INTRODUCTION:

Simple goitre (colloid and multinodular) is the commonest cause of thyroid enlargement world – wide. The solitary thyroid nodule, defined as a palpably discrete swelling within an otherwise apparently normal gland, is usually a benign lesion. Of nodules removed surgically, an estimated 42% to 77% are non – neoplastic colloid nodules, 15% to 40% are adenomas, and 8% to 17% are carcinomas (11,4).

The incidence and pattern of thyroid disease is not known in North – Eastern part of Libya, although the pattern and incidence in Western Libya was reported (1).

In this retrospective study our aim is to analyse thyroid pathology in thyroidectomy specimens in the Benghazi area to identify the pattern of thyroid disease in this part of Libya.

MATERIALS AND METHODS

Benghazi is the second largest city in Libya. The health care system has no private sector and the entire population is covered by the Government Health Services. The various hospitals in Benghazi are affiliated to Al – Arab Medical University, and the catchment area includes the whole of the North – Eastern and part of the South East areas of Libya.

During an 11 – years period, between first January 1981 and 31st December 1991 , 706 patients had thyroidectomy in these hospitals. The decision to operate was made on clinical and laboratory histopathology findings. Subtotal Thyroidectomy was done on patients with large goitres (for cosmetic or pressure symptoms), and thyrotoxic patients, who failed to respond to medical treatment. For the non – toxic solitary nodule, lobectomy was done on suspicion of malignancy. Patients with thyroid cancer underwent total thyroidectomy and, if necessary, neck dissection. Thyroid carcinoma was classified histologically according to W.H.O. classification (15).

RESULTS

The age distribution of 706 patients is shown in figure 1 . Of these, 602 were females and 104 males, a female to male ratio of 6 :1 . Histology types of the removed thyroid are shown in table 1 . Three hundred and fifty patients (49.6%) had simple goitre, 178 (25.2%) adenoma, 73 (10.3%) carcinoma, 41 (5.80%) Grave's disease, 32 (4.5%) various types of thyroid carcinoma are given in table 2 , and age and sex distribution among them table 3 . Female to male ratio for carcinoma was 2.65:1 , of which 39 patients (53.4%) had papillary carcinoma, 23 (31.5%) follicular carcinoma, 7 (9.5%) anaplastic carcinoma 3 (4.1%) medullary carcinoma and one (1.3%) was metastatic carcinoma.

Of 32 patients with thyroiditis, 26 had Hashimoto's thyroiditis, 2 de – Quervain thyroiditis and 4 had non – specific thyroiditis. Age and sex distribution of 41 patients with Grave's disease is shown in table 4 . Among them female to male ratio was 2.4: 1 .

Table (1) : Histology types of 706 Thyroidectomy specimens.

Diagnosis	Number	%
Simple goitre	350	49.57
Adenoma	178	25.21
Carcinoma	73	10.33
Grave's disease	41	5.80
Thyroiditis	32	4.53
Miscellaneous	32	4.53
Total	706	100

Table (2) : Histology types of thyroid carcinoma from 73 thyroidectomy specimens.

Type	Number	%
Papillary	39	53.4
Follicular	23	31.5
Anaplastic	7	9.5
Medullary	3	4.1
Metastiatic Form	1	1.3
Total	73	100

Table (3) : Age and sex distribution of 73 patients with Carcinoma – Thyroid.

Age	Male	Female	Total	%
< 20	1	2	3	4.10
20 – 30	4	13	17	23.28
31 – 40	5	10	15	20.54
41 – 50	4	13	17	23.28
51 – 60	1	5	6	8.21
> 60	5	10	15	20.54
Total	20	53	73	100

Table (4) : Age and sex distribution in 41 cases of Grave's disease

Age	Male	Female	Total	%
< 20	1	3	4	9.75
20 – 30	6	15	21	51.22
31 – 40	2	8	10	24.39
41 – 50	2	2	4	9.75
51 – 60	1	1	2	4.87
> 60	12	29	41	100

DISCUSSION

The commonest thyroid swelling found in endemic areas is simple goitre, which constitutes 50 – 70% of cases (13, 10). In our study simple goitre was found in 49.5% of specimens, and is thus similar to other available figures in literature (13, 10), but higher than reported from Western Libya 44% (1), probably because out – catchment area drains the South – East part of Libya in which endemic goitre is common due to iodine deficiency (5). Benign adenomas accounted for 178 (25.21%) cases, which is less than that reported from Western part of the country (32.52%).

The incidence of carcinoma was 10.3%, which is similar to incidence of carcinoma in Western part of Libya (9.7%) but higher than the 4.25% reported by Campbell et al (3) in the Birmingham series.

The 72% female preponderance in patients with thyroid carcinoma in our study was in agreement with 62 – 81% reported from U.S.A (8). Harda et

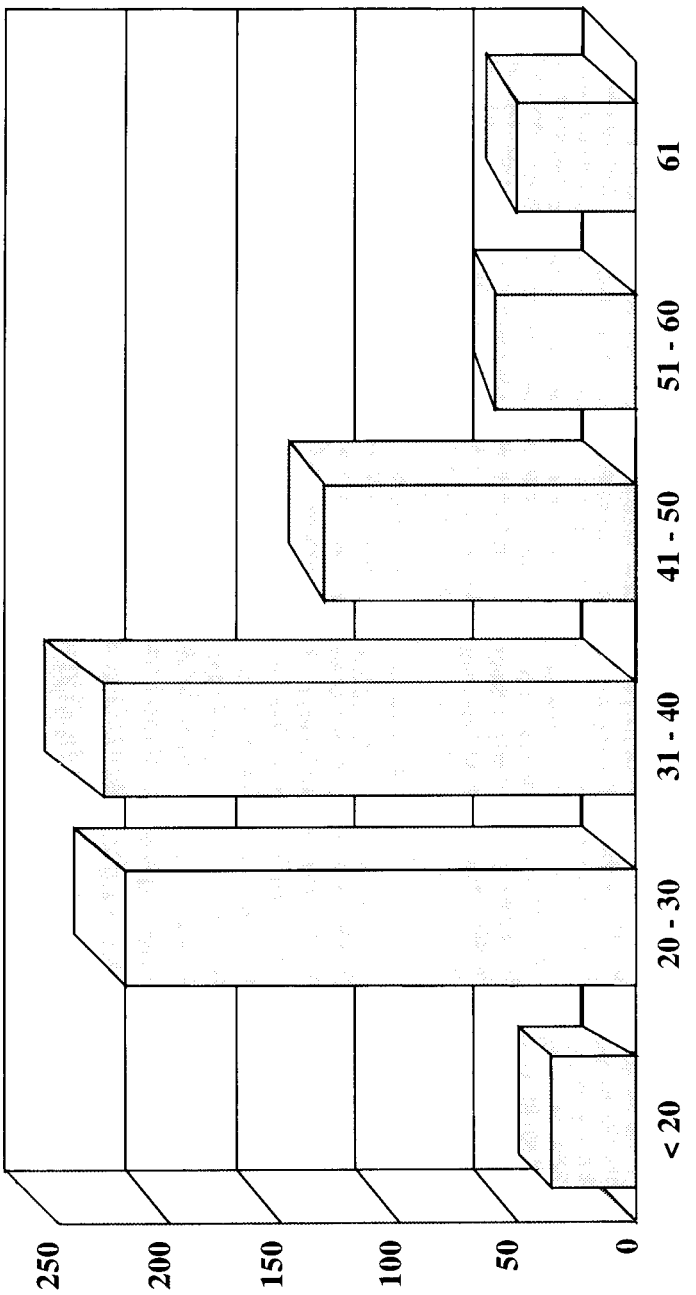

Fig 1. Age distribution of 706 patients that had thyroidectomy

al (1981) (6) reported from Japan, a female preponderance of 91% in thyroid carcinoma. (31.4%), medullary (4.1%) and anaplastic (9.5%) carcinoma in our study (see table 2) was statistically not different from other studies (9). In the U.S.A. papillary carcinoma was reported to occur in 73% (8) and 62% (14) of cases. Beaugie (2) from England reported that papillary caricinomas was 51% all cases of thyroid cancer.

Grave's disease in our study accounted for 5.8% which is similar to the figure reported from Western Libya (1).

There were 32 cases of thyroiditis in this study, out of which 26 (3.6%) were hashmoto's thyroiditis. This is less than other parts of the world, where incidence of Hashimoto's thyroiditis is rising (12). In parts of U.S.A, it is a common cause of goitre (12).

There were four cases of chronic non – specific thyroiditis and only 2 had de – Quervain Thyroiditis. The incidence of thyroiditis is low in our patients as compared with U.S.A. (7).

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Incidence and Management of Cancer Breast in Eastern Libyan Females

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SUMMARY

A review of 104 patients with cancer breast diagnosed at the Oncology Clinic, 7th April Hospital, Benghazi, Libya over a 3 year period (January 1989 to December 1991) is presented. The annual incidence of cancer breast in the Libyan female population at risk (30 – 64 years) was found to be 33.33 per 100,000 . This pattern is similar with Eastern Epurope but higher than other African countries. Cancer breast accounted for 20.25% of all solid tumors diagnosed over the same period, which is lower than Western countries but similar to that of Eastern Europe. The peak age was 41 – 50 years (41.34%) and in premenopausal (50.96%), in sharp contrast with Western countries. Stage II (52.88%) and stage III (30.76%) were the common presentations, as seen in developing countries, like Asia and Africa. The commonest histological finding was infiltration Duct cell Ca. (69.23%). Distant metastasis was found in 50.96%, while local recurrence was recorded in 25.97%, and cases. The most common treatment was surgery (96.15%), with 58.65% cases receiving radiotherapy to locoregional area. CMF/FAC Chemotherapy was given in 66.34% of cases, while antiestrogen was the most common type of hormone therapyion 75.96% of cases. In our series 43.26% cases are under N.E.D. Of the total, 25% of cases died. The prognosis can be improved by providing early and better diagnosis and treatment facilities.

الملخص

تستعرض هذه المقالة 104 حالات من سرطان الثدي لدى النساء الليبيات في فترة ثلاثة سنوات (89 – 91م) شخصت في عيادة الأورام بمستشفى السابع من إبريل ببنغازي لتحديد نسبة حدوثه ومتابعة نتائج العلاج. وتؤكد المقالة على أهمية توفر الامكانيات الطبية للتشخيص المبكر والعلاج للحصول على أفضل النتائج.

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INTRODUCTION:

Breast cancer is the commonest form of cancer in women throughout the world. In 1980 , it was estimated that 572,100 new cases of breast cancer were diagnosed worldwide (12). Of these an estimated 347,900 new cases (60.80%) were diagnosed among the inhabitants of developed countries, and representing 22.9% of all new cancers diagnosed (Excluding non – melanoma skin cancers). Although cancer is traditionally considered a disease of advanced life style and affluence, the developing countries were not spared, with the estimated figure of 224,200 new cases diagnosed, representing 14.2% of the total cancer burden for 1980 (13). Present cancer represented a smaller proportion of cancer in women in Africa (13.4%), and in Asia (17%), with the lowest percentage recorded for Soviet Union (11.8%) and Japan (10.3%) (11).

There is a distinct variation in distribution of cancer breast in various geographical areas of Africa. Libya is situated in North Africa, hence the incidence of breast cancer should be comparable to, and as low as, in most African countries.

In this 3 years retrospective study; incidence, clinical presentation, management and prognosis of cancer breast in eastern Libyan females are presented.

MATERIALS AND METHODS:

This study included 104 female Libyan patients of cancer breast who reported to the Oncology Clinic, "7th April" Hospital, Benghazi. This hospital is one of the biggest teaching hospitals of Al – Arab Medical University, Benghazi, and the Oncology Clinic caters for almost all cancer patients of Eastern Libya.

During the period of 3 years (from 1989 – 90 – 91) a total number of 543 patients suffering from solid tumors reported to the Oncology Clinic, out of which 120 cases were cancer breast. Six cases from them had insufficient data. Another 9 cases were in non – Libyans and one case was in a male patient. These 16 cases were excluded from our study, except that the six cases which had insufficient data were included only in calculation of the incidence.

Medical records of all these patients were reviewed and all data were fed in "Master – Chart". The recorded history included patient's age, menopausal status and clinical features. All patients had routine laboratory investigations, chest X – ray, skeleton survey, mammography, liver function tests, renal function tests, ultrasonography and C.T. scan if needed.

Diagnosis was based on clinical grounds, radiography, and biopsy. The cancer was staged according to UICC – AJC, TNM classification, then grouped in clinical stages; from Stage I to Stage IV.

The appropriate treatment was planned and given according to the stage, and all patients were followed closely at the Oncology clinic.

The exact incidence of breast cancer is difficult to assess since the number of cases seen by us do not reflect the total number as some refused to come to the hospital or were treated elsewhere abroad. To calculate the annual incidence, the female population at risk (30 – 64), of the eastern part of Libya, and the number of cancer patients diagnosed were taken.

RESULTS:

A total number of 543 adult cases of solid tumors reported to the Oncology clinic during 1989 – 90 – 91, out of which 104 cases of cancer breast included in this study. Six cases were not included due to insufficient informations, but they were included in calculating the incidence pattern.

Annual incidence:

The total number of Libyan cases diagnosed in the 3 years was 110 , while the Libyan female population (average) per year at risk (between age 30 – 64 years) was found to be 110,000 females, which gives an annual incidence per 100,000 population at risk of 33.33. The percentage of cancer breast to all adult solid tumors was calculated to be 20.25%.

Age Distribution:

Table 1 shows the age distribution of cancer breast. The peak incidence was 43 (41.34%) between 41 – 50 years of age. The incidence between 31 – 40 years and 51 – 60 years were 25% (26 cases) and 24.03% (25 cases) respectively. Only 3 cases were above 60 years of age (2.88%) while below 30 years of age only 7 cases (6.73%) were found. None of the patients was below the age of 25 years.

Table (1): Age distribution of Cancer Breast

Age in Years	No. Of Patients	Percentage
< 20	NIL	NIL
21 – 30	07	6.73
31 – 40	26	25.00
41 – 50	43	41.34
51 – 60	25	24.03
61 – 70	03	2.88
Total	104	(100.00)

Menopausal Status:

Table II shows the incidence of cancer breast according to the menopausal status. There were 53 women (50.96%) with premenopausal cancer breast while there were 46 women (44.23%) with postmenopausal. Four patients were in perimenopausal, and one patient had hysterectomy prior to cancer breast due to some other medical reason.

Table (2): Distribution of Cancer Breast according to menopausal status

Status	No. of patients (%)	
Premenopausal	53	(50.96)
Postmenopausal	46	(44.23)
Perimenopausal	4	(3.84)
Not known (H/O hystrectomy)	1	(0.96)
Total	104	(100.00)

Site:

Results are shown in table 3 . Cancer breast was leftsided in 59 (56.73%) women, and right sided in 43 (41.34%). Two (1.02%) patients presented with bilateral cancer breasts. Another 9 cases (5 from right and 4 from left side) subsequently developed cancer on contralateral side also.

Table (3): Site of Cancer Breast

Site	No. of patients (%)	
Left	59	(56.73)
Right	43	(41.34)
Both breasts	3	(1.92)
Total	104	(100.000)

Initial Presentation (Clinical Stage):

The majority of our cases 55 women (52.88%), had initially presented with stage II, while there were 32 (30.78%) patients in stage III. Only 15 cases (14.42%) were reported as stage IV with the lowest presentation in stage – I 2 (1.92%) (see table 4)/

Tabel (4): Presentation of Cancer Breast

Stage	No. of Patients (%)	
I	2	(1.92)
II	55	(52.88)
III	32	(30.76)
IV	15	(14.42)
Total	104	(100.00)

Histopathology:

Table 5 shows the various histopathological findings. The most common diagnosis was infiltrating duct cell Ca. in 72 (96.23%) cases. In 13 (12.50%) cases, various combinations with infiltrating duct cell Ca. were found with medullary carcinoma in 6 (5.76%), with lobular invasive in 5 (4.80%), with mucinous Ca. in 4

(3.84%), with Paget's disease in 1 (0.96%) and with Rhabdomyosarcoma in 1 (0.96%). In two cases (1.92%), the exact cell type could not be ascertained as biopsy was done elesewhere and reported as only Cancer Breast.

A total of 53 (56.96%) patients suffered from distant metastasis, either initially or subsequently. Twenty seven (25.97%) patients also presented with local recurrence and one patient (0.96%) suffered from second malignancy as malignant fibrous histocytoma at primary site, after N.E.D. for 8 years. Bones were the common site of metastasis in 29 (54.71%). Sixteen patients (30.18%) suffered from lung metastasis and 8(15.09%) patients suffered from metatatic pleural effusion. The visceral metastasis (liver) was 22.64%. Brain metastasis was diagnosed in 7 (13.22%). Other uncommon sites for metastasis were lymphnodes, skin, eye, adrenal and peritoneal (malignatn ascitis) areas.

Table (5): Histopathological findings of Cancer Breast.

Histopathology	No. of Patients (%)	
Infiltrating duct cell carcinoma	72	(69.23)
Combinations with Infilt. duct cell Ca.	13	(12.50)
i. Carcinoma simplex – 04		
ii. Adenocystic – 03		
iii. Schirrous pattern – 04		
iv. Cammedo's pattern – 02		
Medullary carcinoma	6	(5.76)
Lobular invasive	5	(4.80)
Mucinous	4	(3.84)
Paget's disease with Infilt. duct cell Ca.	1	(0.96)
Rhabdomyosarcoma	1	(0.96)
Not specified	2	(0.92)

Recurrence, Metastatic and Involvement of Another Breast:

Results are shown in table 6 .

Tabel (6): Metastatic presentation of Ca. Breast in 53/104 patients

Type of Surgery	No. of patients (%)	
Bone (s)	29	(54.71)
Lung (s)	16	(30.18)
Pleura (s)	8	(15.09)
Liver	12	(22.64)
Brain	7	(13.22)
Lymph node (3) (High cervical) (Mediastinal)	3	(5.66)
Kin	2	(3.77)
Eye	1	(1.88)
Adrenal	1	(1.88)
Peritoneal	1	(1.88)

TYPE OF TREATMENT (S)

Appropriate treatment (surgery ± radiography ± Chemotherapy ± Hormone therapy) was given to each and every patient according to their clinical stage.

Surgery:

One hundred out of 104 patients (96.15%) we treated by various types of surgery. The most common procedure was simple mastectomy with auxiliary clearance 72 (69.23%). Only 15 (15.38%)

patients had simple mastectomy and 4 (3.84%) patients had lumpectomy only. In 4 patients (3.84%), no surgery was performed, but treated by other modes of treatment (see table 7).

Table (7) : Type of Surgery performed in Cancer Breast

Type of Surgery	No. of patients (%)	
Simlpe mastectomy with axillary clearance	72	(69.23)
Modified radical mastectomy	16	(15.38)
Simple mastectomy	8	(7.69)
Lumpectomy	4	(3.84)
No surgery	4	(3.84)
Total	100	(100.00)

Radiation Therapy:

Radiationtherapy was given to the locoregional area and also to metastatic site (s). A total of 58 (55.76%) cases received adjuvant radiotherapy (postoperatively). About 4000 rads in 4 weeks were given by metavoltage teletherapy. Two (1.92%) cases received radiotherapy after the appearance of surgical recurrence. Only one patient (0.96%) received primary radiotherapy (without any surgery). Forty – three (41.34%) patients did not receive any radiotherapy to the primary site (table 8).

Thirteen patients have also received palliative radiotherapy to various metastatic site (s) (bones, lymph nodes, liver, eyes).

Table (8): Radiotherapy in loco – regional area ≥ 4000 rads in 4 weeks by Megavoltage

Type of Treatment	No. of patients(%)	
Adjuvant to surgery	58	(55.76)
Post – recurrence (surgical)	2	(1.92)
Primary (no surgery)	1	(0.96)
No radiotherapy	43	(41.34)
Total	104	(100.00)

Chemotherapy:

Only 69 (66.34%) cases received six or more courses of chemotherapy while 15 cases (14.42%) could not receive more than four courses of chemotherapy. In 20 (19.33%) cases no chemotherapy was given.

The "C.M.F." or "F.A.C." chemotherapy were the most common regemen applied in these cases studied. In 3 cases (2 pleural effusion and one ascites) local cytotoxic treatment was also given as they were of malignant nature.

Hormone Therapy:

In our study only 79 (75.96%) patients received hormone therapy. Antioestrogen (tamoxifan) 20 mg orally, daily, was given in all cases. In 9 (11.39%) premenopausal patients, bilateral oophrectomy (6 by radiation and 3 by surgical) was also performed.

High dose of progesterone (Depo – provera) was also given in 15 cases (18.98%) after antioestrogen therapy, due to disease progression.

Prognosis:

At the time of this study, 45 cases (43.26%) are under regular follow – ups, out of which 29 (27.88%) cases are without any evidence of disease, while 16 (15.38%) cases are under treatment for metastasis.

A total of 26 (25%) cases died. The exact cause of death could not be ascertained since autopsy could not be done. The prognosis of 33 (31.73%) cases could not be assessed as they did not report for follow – ups for more than one year (table 9).

Table (9): Prognosis of Cancer Breast

Prognosis	No. of patients(%)	
Follow – ups with N.E.D	29	(27.88)
Follow – ups with metastasis	16	(15.38)
Died	26	(25.00)
Not Known (for more than 1year)	33	(31.73)
Total	100	(100.00)

DISCUSSION

In the 3 years (from January 1989 to December 1991), the annual incidence (33.33.) of breast cancer in the Libyan female population at risk (30 – 64 years of age) per 100,000 was high in comparison to other neighhouring countries. Algiers in Algeria had an incidence of 13.2; Cairo in Egypt 23.2; Ibadan in Nigeria, 11.8; Zaria in Nigeria 13.8; Sudan 26.0; and Tunis in Tunisia, 30.5 (11). Similar incidence to Libyan breast cancer was reported from Eastern European countries, like Slovenia in Yugoslavia, 34.21, Warsaw in Poland, 36.49; GDR, 37.41; and Navarra in Spain, 37.86 (17).

Of the highest rated cancer breast countries, 19 were in the areas of North America, where the rates ranged between 60 and 85 per 100,000. Rates in Western Europe were generally between 40 and 60 per 100,000, and in Eastern European populations rates were generally between 20 and 40 per 100,000 (17).

As a Mediterranean region, the incidence rate of Eastern Libya is thus somewhat similar to Eastern Europe countries, but higher than other African countries.

Out of all about solid tumors, the rate of breast cancer in our series was 20.25%, which is lower than what was observed in North America and Western Europe, but similar to Eastern Europe. This study reveals that breast cancer is apparently on the increasing side in female Libyans (6).

The peak age of incidence of cancer breast in this study was between 41 – 50 (41.34%) years of age but incidence above 60 years (2.88%) and below 30 years (6.76%) of age was very low. The incidence of cancer breast was higher in premenopeusal (50.96%) than postmenopausal (44.23%) women. It is in sharp contrast with the findings in United States and Europe (2, 15, 18).

The left side (56.73%) was more involved than the right side (41.34%). There is no clear cut explanation for this incidental findings.

The histopathological findings suggest that the most common presentation in our series is Infiltration Duct cell Ca. (69.23%) which is similar to other studies as observed by Fisher et al (7). In our series, in only 1.92% of cases, no cell type could be ascertained except as cancer breast, since biopsy was done elsewhere.

The most common initial presentation was stage II (52.88%) followed by stage III (30.76%). Presentation in stage IV and in stage I was not common. These finding are similar to those seen in the developing countries of Asia and Africa (3).

In this study, 50.96% patients suffered from distant metastasis. The bone (s) (54.71%) was the most common site, followed by lung (s) (30.18%), and liver 22.64%. Malignant pleural effusion was diagnosed in 15.09%. Brain metastasis was found in 13.22% of patients. Our findings were less than those observed by De – Vitta et al (5). The reason could be that our findings were clinical while findings by De – Vitta et al were of autopsied cases.

A total of 10.57% patients developed cancer breast in the contralateral side. It is not clear whether they are metastasis or another primary (14). One patient also exhibited second malignancy, as malignant fibrous histocytoma, at the primary treated site 8 years after the successful treatment. This uncommon finding was also observed by Valagussa P. et al (16).

Local recurrence after surgery was observed in 25.97% of patients. It was a common problem, as also observed by Aberizk W.J. et al (1).

Simple mastectomy with axillary clearance in 69.23%, was the most common surgical treatment, followed by radiotherapy in stage II and stage III patients (55.76%). The most common chemotherapy regimen was CMF or FAC. Only 66.34% patients could receive six or more courses. Antieostrogens were also given in 75.96% of cases, and 0 premenopausal patients had bilateral oophrectomy. in 15 cases Inj. Depo Provera in high doses were also given in those patients in which disease was not controlled by antioestrogen. These are the treatments commonly applied in Stage II to stage IV (4, 10). Radiotherapy with good palliation was given in 13 patients to various metastatic sites. It is the choice treatment, particularly to bone, brain and solitary liver metastasis.

Prognosis could not be assessed properly as 31.37% patients could not be followed up. In our series 43 (26%) cases are under follow – up of which 27.88% are N.E.D., and 15.38% are under treatment for metastasis. A total 25% of patients died. We were not able to compare our findings with other international findings due to lack of proper follow – ups (8, 9).

CONCLUSION

It is clear from recent reports that breast cancer, the commonest form of cancer in women, is not confined to developed countries. This international cancer burden is equally shared in numerical terms, although not in terms of individual risk, between developed and developing countries. Breast cancer appears to be more common in Libya than previously thought. Hence better facility for early diagnosis and better planning and delivery of treatment are essential to achieve a better prognosis. Patients should also be made aware of the value of follow – ups for their betterment.

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Fine Needle Aspiration Cytology of Brest-Initial Experience in Benghazi , Libya

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SUMMARY

Fine needle aspiration cytology is a method of diagnostic procedure, being adopted more frequently in the diagnosis and management of breast tumours. We present the initial experiences with this technique in the women attending Hawari Hospital, Benghazi. A total of 619 cases were studied of which there were 115 (18.6%) unsatisfactory smears, 184 (29.7%) of fibroadenosis. 117 (18.9%) of inflammatory smears. The results and the histological correlations are discussed.

الملخص

رشف الخلايا المريضة بالابر الدقيقة هو إحدى طرق التشخيص المخبري لتورم الثدي والتي تنال إهتماماً متزايداً، ونقدم في هذه المقالة تجربتنا الأولية لهذه الطريقة من فحص مريضات في مستشفى الهواري ببنغازي.

(619) حالة درست: من بينها 115 حالة (18.6%) كانت رشافاتها غير مجدية... و184 حالة (29.7%) أظهرت مرضاً غدياً ليفياً، و117 حالة (18.9%) أظهرت تورم غدي ليفي، و111 حالة (17.9%) تسرطن خبيث، و92 حالة (14.9%) كانت حالات التهابية عادية، وتقارن نتائج الفحص بالرشف مع نتائج الفحص الخلوي العادي للأنسجة.

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INTRODUCTION:

Fine needle aspiration of tumours was introduced by martin and Ellis in 1930 (8). As early as 1933 . Stewart (9) used this technique to differentiate lesions such as fat necrosis, abscess and fibroadenomas from cancer. Since then, there is a progressive and increased acceptance and practice of aspiration cytology so that it has now become a routine investigation in the management of tumours and tumour – like lesions of the breast (1, 5, 10, 11). Breast diseases, including carcinoma, are frequently encountered in the population in Libya. In the current paper, we describe the initial experiences in fine needle aspiration cytology results in breast diseases in Benghazi.

MATERIAL AND METHODS:

"Hawari Hospital" of Al – Arab Medical University, Benghazi, is an important referral and treatment centre for patients coming from the Eastern half of libya. The majority of patients presenting with breast diseases in Benghazi are treated in this hospital. From January 1991, a regular outpatient breast clinic was conducted once a week and attended by women for screening as well as for treatment.

From January 1987 upto June 1993 , a total of 619 women underwent fine meedle aspiration of breast for various clinical disorders. Majority of the patients (486), belonged to the age group 20 – 40 years. The youngest patient was 11 years old and the oldest was 85 years. After clinical examination, the aspiration was performed using 20 c.c. syringe and a 21 gauge needle, as described by Zajicek (11), and the smears stained by Papaniclaou stain. They were reported in five categories, i.e., unsatisfactory, fibroadenosis, fibroadenoma, malignant, and inflammatory smears. Whenever a subsequent biopsy (excision) or mastectomy was performed, the results were correlated with the cytologic findings.

RESULTS:

Out of 619 cases examined, 115 (18.6%) aspirations were classified as unsatisfactory for a definite opinion. The smears either showed scanty material or artefacts, making a definite opinion impossible. In 73 cases, repeat sapirations were performed (56 had two aspirations and 17 had 3 aspirations) to obtain satisfactory specimens. Among the cases that were diagnostic, there were 184 cases (29.7%) of fibroadenosis, 117 (18.9%) cases of fibroadenomas, 111 (17.9%) cases of malignancy, and 92 cases (14.9%) of inflammatory smears (Table 1 & 2). In the majority of cases of fibroadenosis and inflammatory lesions there was no subsequent surgery. But in the other groups of cases patients underwent surgery, and histopathology was correlated with cytologic findings. Such a correlation was available in only 121 cases. Benign lesions (30 cases) correlated well with the cytologic findings. However, in one case of fibroadenoma, there was a false negative report. It was reported as fibroadenosis. Among the malignant lesions, there were four (4/91 = 4.4%) cases of false negative diagnosis. Out of these, two were reported as unsatisfactory, and one each as inflammatory, and fibroadenosis.

Histologically these cases revealed infiltrating duct carcinomas with Schirrhous pattern. In the case reported as inflammatory, there were large areas of tumour necrosis with inflammation. In one case where cytology was positive, no lesion could be identified on initial histology, but on subsequent re – examination of more sections, an in – situ lobular carcinoma with micro – invasion was identified.

DISCUSSION:

Sensitivity of fine needle aspiration cytology of breast lesions have been reported to be in the range from 82% to 98% as reported by Kline (5). She is of the opinion that statistical differences depend upon the nature of the hospital and the technique adopted. In our series, there were 86 out of 91 cases (95.6%) of malignancy that correlated well with histology. Our series include patients from a general hospital, representing both neoplastic and non – neoplastic conditions. Majority of the patients of benign, and inflammatory lesions do

Table (1) : Distribution of type of smears reported by fine needle aspiration 1987 – 1993

Classification of Smears	Number(%)
Unsatisfactory	115 (18.58%)
Fibroadenosis	184 (29.73%)
Fibroadenoma	117 (18.90%)
Malignant	111 (17.93%)
Inflammatory	92 (14.86%)

Table (2) : Yearwise break – up of aspiration cytology results

Sl. No.	Type of Smears	1987	1988	1989	1990	1991	1992	1993
1.	Unsatisfactory	08	11	19	16	12	38	11
2.	Fibroadenosis	20	37	22	16	14	55	20
3.	Fibroadenoma	16	16	14	12	09	32	18
4.	Malignant	17	27	11	13	15	25	03
5.	Inflammatory	05	16	18	15	05	24	09
	Total	66	107	84	72	55	174	61

series, several doctors, both clinicians and pathologists have performed the procedure and this could be one the reasons for false negative cases, as well as unsatisfactory specimens. We had a total of 115 (17%) of unsatisfactory specimens. There are reports in the literature of obtaining unsatisfactory smears varying from 1 percent to 18 percent (10, 3). As experience increases, the technical improvisation, such as active maneuvers inside the lesion keeping the negative pressure, are sure to decrease the number of unsatisfactory specimens (4).

not undergo subsequent surgery. Thus, we are unable to assess the sensitivity of the technique in these benign lesions. Moreover, due to the lack of proper follow up and migration of patients to other places, a correlation is made impossible. Among the 30 cases of fibroadenomas studied histologically, there was one case (3.3%) of false negative report on cytology. False negative diagnosis was made in 4 out of 91 (4.4%) cases of malignancy. This could be due to Schirrhous nature of the malignancy as well as faulty technique. Several authors have observed that fibrous stroma in the Schirrhous neoplasms has been responsible for false negative diagnosis (1, 5, 7). Other factors that may contribute to this are the smaller size of the lesion, as well as multiple persons performing the procedure (2, 6). In our

This has been an initial experience of fine needle aspiration technique in the diagnosis and management of mammary lesions. With further experience and improvised technique we hope that the technique will be used with better results.

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The Effect of Ramadan Fasting on Plasma Lipids and Lipoproteins

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SUMMARY

During the holy month of Ramadan, fasting is obligatory. Healthy adult Moslems are expected to abstain from food and drink daily from dawn to sunset. The spaced small meals during the day before Ramadan are replaced by one large meal at sunset and a smaller meal before dawn.

We undertook this study as part of assessing the metabolic effects of Ramanan fasting; and we report our preliminary results in this letter.

الملخص

كجزء من دراسة تأثير صيام رمضان على كيمياء الجسم، أظهرت هذه دراسة زيادة ذات مغزى في مستوى الكوليسترول العام في البلازما، وكذلك في أنواع الكوليسترول الأخرى، وزيادة بسيطة في تركيز ثلاثي الغليسريد أثناء الصيام، ولا ندري إلى أي مدى تدوم هذه التغيرات بعد انتهاء الشهر ولا دلالاتها الحقيقية، حيث يتطلب ذلك دراسات أكثر.

Fifty healthy male volunteers, aged between 18 – 63 years, participated in the study. Females were not included because of the possibilities of interruption of fasting, if menstruating.

Blood samples were collected on the first and last days of Ramadan in: EDTA tubes. Lipoprotein fractionation was carried out within 1 – 4 days of blood collection.

Cholesterol was estimated by Zlataks method (*). Triglycerides were estimated by Enzmyatic method (1). Lipoproteins fraction were estimated by Agarose Gel Electrophoresis (6) .

Our results show that at the end of Ramadan the plasma concentrations of total cholesterol, LDL – cholesterol, and HDL – cholesterol were significantly higher than before Ramadan ($p < 0.05$).

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The plasma level of triglycerides and VLDL – TG were slightly higher than before Ramadan levels (> 0.1), as shown is table (1).

Our finding of a slight, non – significant increase in TG and VLDL – TG is in partial agreement with Shourky (7) who reported a

Table (1) : Mean Plasma levels of triglycerides before and after Ramadan in 50 healthy male volunteers.

Variable	Before Ramadan Mean	SEM	After Ramadan Mean	SEM	Significance of change	
Total Cholesterol	222.4	14.00	272.8	11.29	P < 0.05	(S)
Triglycerides	102.1	9.22	120.0	6.9	P > 0.1	(NS)
LDL – Cholesterol	128.1	9.31	157.8	7.47	P < 0.05	(S)
HDL – Cholesterol	73.7	4.67	90.8	3.8	P < 0.05	(S)
VLDL – TG	20.6	1.84	24.0	1.38	P > 0.1	(NS)

(S): Significant (NS): Non Significant

The frequency distribution in these 50 healthy subhects is shown by the frequency histogram.

Our finding of a significant increase in plasma total cholesterol and LDL – cholesterol is in agrement with Shoukry (7), Gwinup (1), Irwin and Feely (4) and Edlestien et al (2). This increase is probably a large – meal effect, as a single large meal increases plasma cholesterol compared with multiple small meals. Our finding of a significant increase in plasma HDL – cholesterol after one month of fasting was not observed by previous studies. Jenkins et al (5) suggested the decreased intake of nutrients per meal lowers cholesterol because a smaller carbohydrate meal causes less insulin secretion. Less insulin in turn means less HmG – CoA reductases, the enzyme responsible for hepatic cholesterol synthesis. A decresase in cholesterol synthesis increases LDL receptors. With resultant lower concentrations of total and LDL – cholesterol, this might mean that fasting increases cholesterol synthesis and decreases LDL receptors which is not a desirable effect.

On the other hand fasting resulted in a significant increase in HDL cholesterol which is of course a desirable effect and could neutralize the effect of increased total cholesterol. The mechanism of this change in HDL – Cholesterol in not clear.

significant increase in TG and VLDL – TG after fasting. These changes in Triglygerides and VLDL – TG are probably due to increased consumption of carbohydrates taken in the form of sweets whose intake is traditionally increased during Ramadan.

For how long do these changes in plasma lipids and lipoproteins last after Ramadan fasting is unclear and should be clarified by further studies.

Yours sincerely, A.M. Swalem, Dept. of Medicne Al – Arab Medical University and Nura N. Balo, Dept. of Laboratory Medicine, Al – Arab Medical University

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Milk: It's Role in the Mucosal Defense Mechanisms (A Review)

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SUMMARY

Infectious diseases especially acute diarrhoeal diseases are the major cause of morbidity and mortality in developing countries partly because of improper hygiene and partly because of malnutrion.

الملخص

هذه المقالة تختص بدراسة علاقة الحليب ومكوناته ومناعة الغلاف الغشائي للأمعاء مع طرح بعض التصورات المستقبلية.

The mucosal surface mucus and microvillus membrane (M.V.M.) act as a physical barrier to luminal antigens and bacteria. Adherence is essential to bacterial colonisation and toxin or antigen penetration.

The quantity and quality of the carbohydrate side chain i.e. glycoprotein and glycolipids, in mucus and icrovillus membrane, may influencethe adherence of bacteria, their toxins and antigens to the intestinal surface.

The microvillus membrane composition changes as the epithelial cell migrate up the villus (1) and also as the animal matures (2) These structural changes, representing one end of the maturation spectrum, may affect the biophysical and biochemical properties of the membrane.

The total protein content of the glycoprotein extracted from mucus in newborn rats is greater than that of the carbohydrate. The carbohydrate portion of the mucin contains small amount of fucose and N – acetyl galactosmamine (3).

The microvillus membrane from newborn

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animals contain higher lipid – protein molar ratio than adults (4) with high fluidity and less organisation (5).

These differences in the arrangement and availability of certain carbohydrate on the side chain may account for the difference in bacterial and antigen penetration and may explain the differences in susceptibility to different microbes.

Human milk on the other hand may accelerate the maturation process of the gastro – intestinal tract. Animal experiments demonstrated that colostrum (6) and mature milk (7) .

Enhance the growth of intestinal epithelium and direct association between maturity of the microvillus membrane and antigen attachment has been established (8).

An important cause of death among young infants in developing countries is neonatal sepsis (9) caused by aerobic gram negative organisms which probably originate from the intestinal flora.

There is indirect evidence that non – toxigenic E. coli are able to exclude toxigenic E. coli from the small intestine probably by competing for the intestinal receptor sites (10).

Human milk contains large quantities of lactose which enhance the growth of lactobacillus bifidus, the predominate colonic bacterial flora in breast – fed babies. Lactobacillus bifidus uses the unabsorbed lactose to produce organic acids that limit the growth of other bacteria. They may also compete with pathogenic micro – organisms for binding sites on colonic epithelium.

Increased sensitivity to E. coli heat stable enterotoxin in immature rat small intestine has been demonstrated (11) and greater number of E. coli were found to be attached to mannose specific surface glycoprotein of intestinal epithelial cells in infant rabbits when compared to adults (12) adherence of V. cholerae to frucose – specific receptors of rat enterocytes was maximal at 6 – 12 days of age, and decreased significantly at weaning (13, 14).

Concentration of N – acetyl, glucosamine a receptor for Shigella spp. And N – acetyl galactosamine a receptor for C – difficile are relatively low in newborn microvillus membranes, shigellosis is absent in the ileum of rabbit younger than 16 days old (15) C.difficile organisms are found in the stool of about 25% of neonates yet clinical diseases is rare (16).

There is abundant evidence for the protective value of human milk in diarrhoeal illnesses (17, 18, 19). This is mainly attributed to its nutritional value and presence of immunoglobulins; particularly secretory IgA (20).

Interaction between milk fat and gastric contents produce large amounts of monolauryl glycerol which has been shown to have antibacterial, antiviral and antifungal activities (21).

Indirect evidence showed that the composition of dietary fat may reduce duodenal trypsin levels (22).

Trypsin enhances the replication of rota – virus (23, 24, 25) and a reduced rate of neonatal infection is associated with high levels of trypsin inhibitory capacity (26).

Human milk contains glycolipids (27) and oligosaccharides (28, 29) which are analogoues to receptors for various micro – organisms on epithelial cells.

Laboratory studies have suggested the possibility of other non – immunoglobulin factors in milk, capable of inhibiting viral replication in tissue culture (30) and preventing bacterial colonisation (31).

These factors could be associated with milk glyolipids or glycoprotein.

Fractionation of human milk by ammonium sulphate precipitation and column chromatography yields a non – immunoglobulin fraction which has been shown to protect rabbits against enterotoxin – induced intestinal fluid secretion. preliminary studies showed that the inhibitory activity was extracted by chloroform and methanol which suggest the involvement of lipid structures (32).

Human newborn infants are vulnerable to lethal infection by listeria monocytogenes which is able to survive intra – cellulary but pretreatment of neonatal rats with lipopolysasccharides protect

them against a lethal challange with this organisms (33).

A glycolipid or a glycoprotein compound in the non – immunoglobulin fraction of human milk inhibits the adherence of certain enterotoxigenic E. coli strains to guinea pig intestinal tract (31) and also neutralise and kill Giardia lamblia (34, 35, 36).

These studies indicate that it may be possible to reduce acute diarrheal disease in infants by improvement of nutrition and promotion of health education for the long term. We could also change the composition and the fatty acid profile of human milk and small intestinal microvillus membranes; using a variety of diets (37, 38, 39, 40, 41). Recent preliminary studies support this hypothesis (40, 41).

For the short term, we could use, as adjuvant to oral rehydration fluids, fractions of human milk to exclude or reduce the colonisation by several microbes, the specificity of which depends on the microbe and the structure of the receptor.

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Current Opinions on the Clinical Importance of Alpha-Feto Protein - (A Review)

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SUMMARY

This is a review article on the clinical importance of alpha -- feto – protein (AFP). Since 1944 when AFP was discovered, the interest in this serum protein has increased enormously especially in biochemistry, biosynthesis, metabolism and importance in early diagnosis of disease such as primary hepatocellular carcinoma.

الملخص

تتحدث هذه المقالة المرجعية حول أهمية البروتين الجيني ألفا.
منذ أن اكتشف هذا البروتين سنة 1944؛ والاهتمام به في ازدياد مستمر.
وتتحدث المقالة أيضاً عن تاريخ اكتشاف هذا البروتين وتركيبه الكيمائي، وتمثيل الغذاء، وأهمية هذا البروتين في التشخيص المبكر لبعض الأمراض وخاصة سرطان الكبد الأولي.

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INTRODUCTION:

Recent years have witnessed rapid development of knowledge of fetal biology. The latest achievements in this field provide new possibilities for the early diagnosis of various diseases. The discovery of a number of fetal proteins aroused great interest in this subject. Although numerous facts about fetal proteins have been discovered, some dilemmas still exist and the results gained are far from being definite and final. Among these proteins the one first discovered, alpha – feto – protein (AFP) has been most investigated.

The appearance of fetal proteins in the serum represents a physiological phenomenon at the embryo stage. Their development in adults is therefore, presumed to be pathological.

AFP was first discoered in the serum of a goat in 1944 by pedersen (7) and its presence in the serum of a human was confirmed in 1956 by Bergstrand and Czar (3). Abelev et al in 1963 (1) showed experimentally that AFP was present in the serum of mature rat with a transplantable hepatocellular carcinoma. Abelev et al also confirmed that the hepatocellular carcinoma of the mouse synthesized and secreted AFP into the blood. When Tatarinow 1964 (9) detected AFP in the serum of patients with hepatocellular carcinomas, the interest in this serum protein increased enormously. Efforts were also made to confirm the existence of other fetal proteins in the serum. It was also logical to assume that they might be used for diagnostic purposes and that a relation between the pathogenesis of the tumor and fetal biology will finally be found.

Biochemistry of AFP

AFP is a sour plycoprotein of the type of the alpha – 1 globulin. Its molecular weight in humans is about 72 KDa (Klose and Schmiegel; 1990) (6). This protein seems to be a unique characterstic of the species although there is crossreaction between fetal proteins of different species (Rouslathi and sappala; 1971) (8). Several specific fetal fetal proteins are obtained through electrophoresis, alpha – 1, beta – 2, and gamma – feto – protein. AFP is distinguished from them by its physical and chemical feature, and by its antigen composure. It can also be differentiated form other carcinofetal antigens, such as CEA.

In 1972 Alpert (2) discovered two molecular forms of AFP. They were again found in the serum of patients with primary liver cancer submitted to the investigation and independently in the serum of a fetus, at the stage of the tumor or embryo genesis. It is still obscure whether these are two genetically different forms or are only the results of a modification in the molecular structure. There is also a possibility that these forms resulted from varius changes during AFP metabolism.

Biosynthesis of AFP

In humnas, biosynthesis is mainly localized in the fetal of the liver and in cancer tissues, particularly in primary cancer of the liver (Trichopoulos 1980) (10). AFP is also synthesized in tumors of the germinal cells, and in teratoblastomas. In 1972 Gitlin and Perricelli (4) proved its synthesis in the amniotic sac, and in the gastrointestinal organs of a fetus.

Metabolism of AFP

AFP metabolism has still been poorly investigated, It occurs in greatest amounts during the first trimester of intrauterine life and then decreases gradually till it finally disappears from the blood several days after birth. AFP is secreted transplacentally, so can be found in the serum and urine of a pregnant woman. It can also be found in the ascitic fluid of patients with malignant tumors.

Clinical Importance of AFP

According to Ward 1987 (11) the half – life of AFP is 3.5 – 4.0 days. Its. physiologic function is still obscure. Increased values in the serum in adults appear most frequently in patients with primary liver cancer, teratoblastoma of germinal cell tumor. However, there are also considerable variations depending on sex, age, geographic distribution and between races and individuals. Statistical analysis shows that AFP positivity ranges from 33 – 95%, depending on the method used.

In Yugoslavia AFP positivity was present in 69% of the poplulation according to Hamid 1991 (5). In the black population of the Bantu clan it

was found in 87% of the cases while it was found in 93% of the Chinese population in Formosa. AFP positivity was present in 40% of the white population in the USA. In children less than 14 years of age, AFP positivity was found in 90% while in older children and adults it was in 70% of the cases.

According to Trichopoulos 1980 (10) statistics show that males make up 45% of the total of AFP positives while the females make up only 20% There is no absolute correlation between the histologic type of the primary liver cancer, its size and its speed of growth and AFP presence in the serum.

There are several theoretic presumptions about the cause of AFP in the serum. Abelev 1963 (1) has suggested three possibilities based on his experimental results. According to the first one, AFP appears only in proliferative liver cells while it remains suppressed in other stages of the cell cycle. This hypothesis could explain its appearance in oncogenesis.

The second hypothesis starts from a presumption that the hepatocyte differentiation depends on the number of its mitosis. Some experiments have led to the assumption that AFP synthesis is characteristic of the early stage of hepatocyte differentiation when the cell can be called a hepatoblast in contrast to a hepatocyte.

AFP synthesis decreases as the number of mitoses increases. The increase in the amount of synthetisized albumin, transferrin and other proteins characterizing the plasma of adult animals is evident at that time. Different hepatomas can therefore be said to correspond to different stages of the hepatocyte development, i.e., its differentiation. This suggestion could explain the positive correlation between AFP production and «hepatocytoma» and «hepatabastoma» that has been found experimentally. The hypothesis, however, does not exclude proliferation of the liver parenchyma without a corresponding increase in the synthesis of AFP. Since the author mentions this possibility that has also been been confirmed in vitro, it is necessarily concluded that hepatocytes are able to retransform to the stage of hepatoblasts, and this is hardly believable. This, howerver, would be necessary if the induction of AFP synthesis in hepatotectomized animals or the resynthesis of AFP in vitro after transplantation of the AFP negative (fifferentiated) hepatoma are to be explained.

The third hypothesis leads to the presumption that hepatoblasts (AFP producing cells) and hepatocytes (Adult protein producing cells) are terminal elements of various branches originating from a common progenitor – a basic liver cell. From this point of view a hepatoma can be considered to be composed of basic cells capable of developing into a hepatoblast or a hepatocyte depending on the type of the tumor.

AFP producing tumors are related to hepatoblasts by their biologic and antigenic characteristics while the so called «AFP negative tumors» are considered to be more closely related to a hepatocyte. AFP and albumin synthesis are thus believed to take place in differnt cells. It is also possible that their mutual relationship may change and this would not require a great variability of the antigen structure. It is suggested that these cells change considerably in their life time. The life span of hepatoblasts is longer than that on hepatocytes.

There is also a hypothesis that explains the appearance of AFP by a genetic disorder. Thus, in normal healthy persons the gene conducting AFP production in the late stage of fetal life and in adults is normally suppressed, but in pathological states, the gene is released in some way and it further governs AFP synthesis.

The first papers in this subject reported a large proportion of AFP positive cases among patients with primary liver cancer, terablastoma or germinal cells tumor. Later papers, however, pointed to the appearance of AFP in further disorders of the liver and some other organs. Since a malignant process is involved in the majority of cases, there arises the question of the role of metastasis in the liver in these malignancies. Regarding «non – malignant» disorders of the liver, it is obvious that they affect the liver

parenchyma directly, or do so during the course of the disease.

Constantly improving methods of greater sensitivily are associated with loss of specificity. Similar dilemmas exist concerning CEA determination. The problem arises whether to apply a more sensitive method that will sometimes give a false positive result and thus lead to further complex diagnostic procedures and even surgery, or stick to the less sensitive methods that fail to identify some cases but are more specific. The authors plead for raising the lower limit of normal values. Bearing in mind these considerations regarding specificity in addition to primary liver cancer, teratoblastoma and germinal cells tumor, has been found in the following diseases:

1 – Acute viral hepatitis, chronic hepatitis, liver cirrhosis.
2 – Hyperbilirubinemia in newborn infants.
3 – Adenocarcinoma of the gastric with metastasis in the liver.
4 – Adenocarcinoma of the gallbladder with or without metastasis in the liver.
5 – Carcinoma of the pancreas with metastasis in the liver.
6 – Carcinoma of the colon with metastasis in the liver.
7 – Carcinoma of the prostate with metastasis in the liver.
8 – Argentagginoma with metastasis in the liver.
9 – Infective monoucleosis.
10 – Hemochrimatosis.
11 – Sclerodermia.
12 – Dermatomyositis.
13 – SLE.
14 – Malignant lymphoma.
15 – Lung cancer with metastasis in the liver.
16 – Breast cancer with metastasis in the liver.
17 – Abnormal pregnancies in the first trimester.

Using immunological and chemical methods analysis of the AFP produced in these conditions, revealed no differenes between it and that produced in the fetus or in hepatic tumour. But it is early to state any definite opinion about the similarity of these proteins since the investigations are still at an early stage.

Inspite of such a wide range of AFP distribution, it remains true that APF is most frequently found in liver cancer, teratobalstoma or germinal cells tumor. Statistics also show that values of AFP are higher in primary liver cancer than others. It is also important to follow its level. In hepatitis, for example, the AFP level can be temporarily increased in acute viral hepatitis. In cases with high AFP levels that are steadily increasing, a primary liver cancer should be suspected, while persistent moderately increased AFP levels point to cirrhosis. This scheme is not to be strictly followed, since any combination of these diseases can change AFP levels in the serum. In the last few years a growing number of scientists have been examining the problem of evaluating the diagnostic importance of AFP and it has been showed that AFP values, in cases with primary liver cancer, can vary from normal to several hunderd milligrams. Determination of AFP levels in the serum is of diagnostic importance, eg., making the differential between biliary and neonatal hepatitis. If high concentrations of AFP are found prenatally in a pregnant woman, they can help in the diagnosis of various malformation of a fetus.

Determination of AFP levels is also of great prognostic value, especially in surgery. If after a removal of the hepatic tumor, the AFP level decreases and remains low for long, it is a good prognostic sign. In cases of fulminant hepatitis AFP is found to correlate with the severity of the disease and its prognosis. This is explained by a regenerative capacity of the liver after necrosis during the acute stage.

There is not unanimity of opinion concerning the appearance of AFP during regeneration of the liver. Some authors think such appearance is impossible in humans while the others such appearance is impossible in humans while the others believe that this is the only possible way to explain the appearanve of AFP after necrosis of hepatocytes. There still exist numerous dilemmas. For example, although the appearance of AFP in the cells of tumors has been confirmed by the immunofluoresence method, «gene depression» is

considered possible not the cells producing AFP in the tumor but in hepatocytes. It is therefore, of clinical importance to estimate AFP in the serum.

CONCLUSION

It is generally concluded that determination of AFP levels in serum had considerable diagnostic imortance, but only as one of a series of diagnostic procedures. The sensitivity of determination depends on the method used. There is consensus of opinion on these methods. Less sensitive ones are less so.

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Asthma : Pathogenesis and Management (A Review)

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SUMMARY

Asthma is a chronic illness that characterised by increased responsiveness of tracheobronchial tree to multiplicity of stimuli. It is manifested physiologically by widespread narrowing of the tracheobronchial tree, and clinically by paroxysms of dyspnea, cough and wheezing, that resolve spontaneously or with therapy. It is an episodic disease, acute exacerbation being interspersed in terms of features that purportedly have a role in its pathogenesis and pathophysiology, airway inflammation and bronchial hyperresponsiveness (34).

Asthma is a common disease affecting approximately 3 to 5 percent of the population. The prevalence and severity of asthma are rising (19). The mortality from asthma has been increasing. The causes of this increase has not been established. Possible reasons include adverse response to B2 – agonist therapy, improper assessment of the severity of the episode by the patient, physician or both (26); and inadequate treatment in the hospital. In this article, we shall briefly review pathogenesis and management of asthma.

الملخص

الربو مرض مزمن يتميز برد فعل متزايد في القصبات الهوائية لعدة مؤثرات ينتج عنه تضيق في القصبات مما يتسبب في أعراض مختلفة كصعوبة التنفس والسعال والأزيز الربوي، وقد تزول الأعراض تلقائياً أو بالعلاج. في هذه المقالة الاستعراضية، يتناول المؤلفان الموضوع من حيث أسبابه وطرق علاجه.

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ASTHMA IS AN INFLAMMATORY DISEASE

Fatal asthma is associated with marked inflammatory changes in the submucosa of the airways (16). Inflammation is present even in patients with very mild asthma (30, 7). Biopsies of bronchial tissue from patient with asthma have shown that infiltration by inflammatory cells, particularly eosinophils and lymphocytes, and epithelial shading are prominent features.

Thet main pathologic features of asthma are the lack of neutrophils and the dominance of eosinophils in the exudative phase, the sparsity of phagocytic – cell infiltrates, and the absence of granulation tissue and fibrosis.

PATHOPHYSIOLOGY

A complex interaction of various types of cells which found in the airways of patient with asthma, lead to the elaboration of chemical mediators that produce an intense local biochemical reaction, which can be neurally amplified (14, 27, 2).

Mast cells play an important role in this process; when stimulated, mast cells degranulate and release histamine and arachidonic acid metabolites, such as leukotrienes and prostaglandins. Platelet activating factor (PAF) and bradykinin are also generated. This mediator cascade can cause the bronchial smooth muscle to contract, enhance the vascular permeability leads to mucosal edema, and increase the production of mucous as well as interfere with removal. Simultaneously, chemotactic compounds such as neutrophil, and eosinophilinduced chemotactic factors of anaphylaxis, leukotriene B4, PAF, and hydroxyeicosatetraenoic acids elicit a migration of neutrophils and eosinophils to the site of degranulation and may activate platelets (28, 15, 46). This second phase takes many hours to develop. Once it occurs, the cells involved, as well the resident macrophages, can provide more arachidonic acid metabolites and so enhance both the immediate and delayed phases by initiating the feedback loop. This second phase takes many hours to develop. Once it occurs, the cells can also elaborate a family of molecule called histamine – releasing factors, which can interact with cells in the mast cellbasophil series and further amplify the inflammatory response.

Patients with atopic asthma have also been found to have activated T – helper cells in their airways (39). These cells, alongwith endothelial cells and epithelial cells, fibroblasts, and macrophages, synthesize signal proteins referred to as cytokines, whose receptors and biological functions regulate the response of the other cells, the inflammatory cascade.

Interleukin 3 and interleukin 5 selectively increase the adherence of basophils and eosinophils respectively, and interleukin 2, interleukin 3, interleukin 5, and GM – CSF prolong survival of eosinophils.

Eosinophils are very prominent cells in asthma. In fact, the pathology is often termed "chronic eosinophilic desquamative bronchitis". It is well known that blood and sputum eosinophils are often, but not invariably found in association with most form of asthma. Proteins released from eosinophil granules, such as major basic protein and eosinophil. Cationic protein, may be toxic to the airway, epithelium and is responsible for the sloughing of epithelial cells (8). This disruption of the epithelial barrier on the mucosal surface of the airway may in turn contribute to airway hyperresponsiveness (25). through a variety of postulated mechanism. Eosinophils have the capacity to generate comparable quantities of PAF to that produced by neutrophils.

It is now appreciated that T – cell derived product, which play a vital role in eosinophil maturation, also affect the mature cell. For instances, both GM – CSF and IL – 5 activate mature eosinophils in terms of increased cytotoxicity and oxidative metabolism and prolong life of eosinophils. Recruitment and activation of eosinophils is strongly inhibited by cortocosterids, an effect that could explain the efficacy of these drugs in modifying late – phase bronchoconstriction.

A possible role for neurogenic mechanism in asthma has long been recognised. However, earlier interest in abnormalities of the autonomic nervous

system has recently shifted to interest in neuropeptide tachykinins, such as substance P and neurokinin A, which are released from sensory nerves in the airways and can produce bronchoconstriction and secretion of mucous (4). Because airway tachykinins are normally degraded by a neutral endopeptidase present in airway epithelial cells, damage to the surface epithelium may be associated with an exaggerated effect of these tachykinins (33).

INFLAMMATORY MEDIATORS

Many inflammatory mediators have been implicated in Asthma (3, 29, 12), and may contribute to various features of asthmatic response, such as bronchconstriction, microvascular leakage, and mucous secretion. Inflammatory mediators also contribute to bronchial hyperresponsiveness. PAF also play an important role in pathogenesis of airway hyperresponsiveness. PAF, released from mast cells, eosinophils, and other inflammatory cells, is a membrane – derived lipid mediator with a variety of effects, including bronchoconstriction, chemotoxis for eosinophils, secretion of mucus and increased bronchial responsiveness (42, 35).

CLINICAL ASSESSMENT

The clinical assessment of patient with asthma is best performed by objective measurement of forced expiratory air flow, using either a spirometer or a peak expiratory flow meter. Decreases in FEV, and the ratio of FEV, to forced vital capacity constitute the typical spirometric pattern of air flow obstruction.

THERAPEUTIC IMPLICATION

Asthma represents a special type of inflammation of the airway that leads to contraction of airway smooth muscle, microvascular leakage, and bronchial hyperresponsiveness, resulting in intermittent wheezing and coughing. So treatment aims, reducing the inflammation and promote bronchoconstriction. Antiasthma drugs can be classified a as bronchodilator or as anti – inflammatory drugs.

BRONCHODILATOR DRUGS

These drugs act primarily by reserving the contraction of airway smooth muscle, B – adrenergic agonist are effective mast – cell stabilizers.

B – ADRENERGIC AGONIST DRUGS

B – Adrenergic agonists are most effective bronchodilator. Activation of B2 adrenergic receptors on airway smooth muscle leads to the activation of adenylate cyclase and to an increase in the intracellular concentration of cyclic AMP. This increase leads to the action of protein kinase A, which inhibit the phosphorylation of myosin and lower intracellular ionic calcium concentration, resulting in relaxation. They relax the smooth muscle of all airways, from the trachea to terminal bronchiole.

They relax the airway irrespective of the spasmogen involved, thus protecting against all bronchoconstrictive challenges. B – Adrenergic agonist may inhibit the release of mediator from mast cells in the airway (10, 23) and release of acetyl choline from post – ganglinoic cholinergic nerves in the airways (38).

B – Adrenergic agonists do not inhibit either the late response to allergens or the subsequent bronchial hyperresponsiveness (12). B – Adrenergic agonist do not have an inhibitory effect on either macrophages in the human lung or eosinophils inflammatory cells that have been implicated in both the late response and bronchial hyperresponsiveness (11).

Inhaled selective B2 – adrenergic agonist (albuterol, terbutaline, fenoterol, and bitoterol) have a rapid onset of action and are effective for three to six hours when the asthma is not severe. Long acting B – adrenergic agonist (Salmeterol) may be effective for more than 12 hours and useful in treating nocturnal symptoms (45). Inhaled B – adrenergic agonists are indicated for the short – term relief or bronchoconstriciton and are the treatment of choice for acute exacerbation of asthma. Orally administered B – adrenergic agonist are less useful because of the increased incidence of side effects.

SIDE EFFECTS

Untoward effects are common when B – adrenergic agonist are given by nebulizer or orally and uncommon when they are given by inhalation. Tremor, tachycardia, and palpita – tions, are common. At higher doses hypokalaemia occur. Even after regular long term use tolerance to the bronchodilator effects.
B – adrenergic agonist does not develop.

THEOPHYLLINE

It is less effective bronchodilator than B – adrenergic agonist.

Initially, it was thought to cause bronch – odilation by inhibiting the production of phosphodiesterase, thus increasing the concentration of intracellular cyclic AMP. Another mode of action is antagonism of adenosine receptors, which does occur within the therapeutic range. It also causes inhibition of the intracellular release of calcium and stimulation of catecholamine release. Theophylline inhibit, the late response to allergens (36). It does not prevent the bronchial hyperresponsiveness that follows allergens exposure and does not inhibit the release of mediatiors from eosinophils.

CLINICAL USE

The introduction of slow release preparation of theophylline has given a new impetus to the use of these drugs in treating asthma. Sustained release preparation have been particularly useful in treating nocturnal asthma, as therapeutic plasma concentration of theophylline may be maintained overnight by giving a single dose in the evening, sustained release theophylline preparation can be given twice daily and provide greater efficacy, fewer side effects, and improved compliance compared with immediate release theophylline preparation (43, 22).

ANTI – INFLAMMATORY DRUGS

Chronic inflammation appears to be central to the pathogenesis of asthma, it is logical to use agents that suppress this process, such as corticosteroids and cromolyn sodium.

CORTICOSTEROIDS

Corticosteroids are effective in suppressing the inflammation induced by asthma. Steroids act on various comoponents of the inflammatory response in asthma (31). Steroids do not inhibit the release of mediators from mast cells in the human lung (41), although they do inhibit the release of mediators from macrophages and eosinophils. These variations explain why steroids, at least in single doses, do not block the early response to allergens, but do block the late reponse and subsequent bronchial hyperresponsiveness (12), as well as reduce the bronchial hyperresponsiveness when given on an long term basis (5). Steroids given by inhalation are more effective than orally administered steroids in reducing bronchial hyperresponsiveness, suggesting action on cells close to the lumen of the airways. Steroids also inhibit the influx of inflammatory cells into lung after exposure to allergens and reduce peripheral blood eosinophilia (6). Steroid induces the synthesis of lipocortin, which inhibit the production of phospholipase A2 and thus leads to decrease in the synthesis of prostaglandins, leukotrienes, and platelet activationg factor (20).

Steroids given by inhalation have proved to be a great advance in the management of asthma. Beclomethasone, triamcinolone, Flunisolide and budesonide are active topically and reduce frequency of acute episode of asthma and the need for concurrent medication, lessen the requirement for the oral steroids and lower airway reactivity (9, 37). The clinical response to steroid given by inhalation is doserelated and some patients respond only to higher doses (> 500 ugm daily) (41). High dose aerosolized steroids is commonly used to control unstable asthma (41). This approach diminishes the need for oral glucocorticosteroids.

Orally administered steroids, such as prednisone, prednisolone, methyl prednisolone, are still necessary to control asthma in a minority of patients, but their use is associated with side effects when the daily dose exceeds 10 mg.

Side effects are uncommon when low doses of

steroids (<400 ug daily) are given by inhalation, but they become more frequent at higher doses. Side effects include oropharyngeal candidiasis and dysphonia. In children higher doses (> 400 ug daily) may cause some adrenal suppression. Orally used steroids cause hypertension, diabetes, myopathy, osteroporosis, skin fragility, cataract and psychiatric disturbance.

CROMOLYN SODIUM

Cromolyn given by inhalation is capable of preventing or controlling asthma in some patients, but is less effective than steroids given by inhalation. It inhibits the release of mediators from mast cells and so it inhibits the immediate response to allergen and exercise. It also prevent the late response. It protects against exercise induced asthma.

Children with predominantly allergic asthma have a better response to cromolyn therapy than adults. Cromolyn is the antiinflammatory drug of choice in children because it has few side effects. Drug is well tolerated and minor side effects include throat irritation when powder is inhaled.

Other anti-inflammatory and immunosuppressive drugs recently used for asthma are methotrexate and cyclosporine .
Initially promising results with low dose methotrexate as a steroid - sparing agent (32) have been tempered by other data showing no beneficial effect (17). Treatment with cyclosporine , which acts mainly by inhibiting the activation of T lymphocytes, was shown to improve flow rates and decrease the frequency of exacerbation in a placebocontrolled , cross over trail (1).

Potential future therapy for asthma include agents that act against proposed mediators, especially leukotrienes and PAF, by either inhibiting their synthesis or antagonising their action. Promising preliminary results have been obtained with leukotriene antagonists (18, 44) and with blockers of the enzyme 5 – lipoxygenase, a key enzyme in synthesis of leukotrienes (24). Similarly, preliminary results, with PAF antagonists have shown decrease accumulation of eosinophils or a reduction in bronchial hyperresponsiveness after allergen challenge (35). More data regarding the usefulness of these new approaches to asthma therapy will undoubtedly be forthcoming in the near future.

FRAMEWORK FOR MANAGEMENT

On the basis of current knowledge of the pathogenesis of asthma , and the pharmacology of anti - asthma drugs , it is now possible to provide clear guidelines for stepwise asthma therapy . The severity of patient's asthma is assessed , at first , and advice on the avoidance of the trigger factors like allergens , occupational sensitizers , non - steroidal anti - inflammatory drugs and B - adrenergic antagonist and other inciting factors must be given .

Step 1 :

For patients with mild asthma who have occasional symptoms, such as those with exercise – induced asthma, should be treated with exercise – induced asthma, should be treated with an inhaled B2 agonist taken on an "as required' basis and increasing dose as symptoms dictate (e.g.salbutamol, 200, ug).

Step 2 :

If symptoms become more frequent requiring the use of an inhaled bronchodilator more than once a day, or if nocturnal asthma symptoms are occuring, then antiinflammatory treatment should be started, low – dose steroids given by inhalation (< 500 ug daily) or cromolyn. Steroids given by inhalation should decrease the need for bronchodilator treatment.

Step 3 :

If asthma symptoms are not controlled then the dose of inhaled corticosteroids should be increased. High – dose steroid inhalation have proved very useful in controlling chronic asthma, daily doses as high as 2 mg do not produce systemic effect in adults.

Step 4 :

Patients whose asthma remains poorly controlled, or who have nocturnal symptoms in spite of regular treatment with high dose inhaled corticosteroids, may benefit from the slow release oral preparation of B – adrenergic agonist. Slowrelease oral preparation of theophyline should be used as third line drug to provide additional control of symptoms. Theophyline is particularly effective in controlling nocturnal exacerbation of asthma when given as a single dose in the evening. Ipratropium bromide may offer additional bronchodilation in a few patients.

Step 5 :

A few asthmatic patients will need long term oral corticosteroids in addition to the above anti – asthma treatment. The lowest dose necessary to control asthma should be determined.

Sometime a patient's asthma may be so severe that his or her symptoms remain poorly controlled in spite of regular oral prednisolone and above mentioned drugs. In the these patients additional measures may require like high dose B2 agonist treatment given via portable nebulizer. Subcutaneous admininstration of B2 agonist via a portable syringe driver or immunosupperssant treatment with low – dose methotrexate.

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Immature Cervical Teratoma in a Newborn (Case Report)

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SUMMARY

This presentation reports an unusual case of a large cervical teratoma in a newborn who presented with acute respiratory distress. Prompt surgical excision of the tumour led to complete recovery. The significance of this case lies in the fact that though clinically and intraoperatively no evidence of malignancy was found, careful histopathological search revealed immature elements in the excised tumour. On the basis of this the patient was carefully followed during the post – operative period. He has not developed any evidence of recurrence or metastasis either in the cervical lymphnodes or in distant organs.

الملخص

هذا تقرير عن حالة غير عادية لحدوث ورم مسخي كبير في رقبة وليد حديث سببت له ضائقة تنفسية زالت تماماً بإزالة الورم جراحياً. وتأتي أهمية هذه الحالة في عدم ظهور نوعية الورم عند الفحص الاكلينيكي وأثناء الجراحة.
إلا أن الفحص النسيجي المرضي أظهر عناصر خبيثة غير ناضجة في الورم المستأصل مما استدعى متابعة الحالة جيداً حتى تأكد عدم انتشار الورم في الغدد اللمفاوية بالرقبة أو بالأعضاء البعيدة.

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INTRODUCTION

Cervical teratoma is a rare tumour in the newborn. Upto 1983 only 136 cases of cervical teratoma were reported in English literature (1). They form less than 5% of the teratomas encountered in childhood (1, 4). The cervical teratomas are clinically important as they need prompt surgical intervention to save life and have to be followed carefully even after complete excision of the tumour. In this paper we present a successfully treated neonate with a huge cervical teratoma in whom pathological examination revealed immature elements.

CASE REPORT

M.J., a day old infant born with a large swelling infront of the neck and respiratory distress, was transferred from the nursery of "Jamahiriya" hospital. His birth was normal and uncompli – cated. Soon after delivery, however, he became cyanosed and dyspnoeic.

On examination, he weighed 3.2 Kg and was cyanosed and severely dyspnoeic with slight improvement of respiratory distress on extending the the neck.

Local examination revealed a large swelling in the anterior aspect of the neck occupying the entire area between the chin and the angle of the mandible on the left side above and suprasternal notch below. Laterally the margin of the tumour could be felt at the anterior margin of the left trapezius. Large engorged veins were seen over the surface of the swelling. The consistency was variable with cystic and firm to hard areas. The trachea was shifted towards the right side and the carotid pulsations could not be felt. The other systems were normal.

Haematological and biochemical investigations were within normal limits. X – ray of the neck in antero – posterior and lateral views showed compression and extreme deviation of the trachea on the righet side. Chest x – ray was normal.

The patient was promptly intubated and was kept on intermittant positive pressure ventilation. Meantime, blood was cross matched and was kept for the operation. Under general anaesthesia, a large incision extending from the anterior border of the trapezius muscle on one side to the otner side was made. The skin flaps were reflected. The swelling was well capsulated and could be separated easily from the organs such as trachea, oesophagus, carotid sheath and recurrent laryngeal nerve. The swelling was not infiltrating the surrounging tissues or structures. The thyroid lobe on the left side could bot be identified. Also no definite vascular pedical could be seen. The tumour was completely separated and excised. After surgery, The patient was kept on assisted ventilation for 24 hours following which he recovered fully. There were no complications during the immediate post – operative period.

Histopathological examination of the excised tumour revealed tissues derived from all three germ layers. Predominant primitive neuroepithelial three germ layers. Predominant primitive neuroepithelial elements with formation of rosettes (Fig. 1), immature cartilage and embryonal mesenchymol tissues were seen. In other areas cysts lined by tall columnar epithelium and glandular structures were also present (Fig. 2). Frequent mitotic figures were identified.

The patient was followed up for 1 1/2 years and was found to be in normal health.

DISCUSSION

Cervical teratomas have a clinical as well as pathological significance. Clinically their presentation is dramatic with a large swelling infront of the neck and acute respiratory distress. They have to be distinguished from other cervical swellings such as cystic hygroma, congenital thyriod goiter and branchial cleft cysts. These swellings, unlike cervical teratoma, do not need urgent surgical intervention. The mortality reaches 80% in unoperated cervical teratoma but if operated immediately it is reduced to 15% (1).

Because of their huge size, cervical teratomas compress the deeper structures, especially the trachea, causing acute respiratory distress. This requires prompt and proper management in the early period. In our patient, early excision led to immediate relief of symptoms. If there is no improvement after the intubation of the patient, pulmonary hypoplasia should be suspected (1).

In the past, various terms have been used to describe these tumours. If the tumour is supplied by the vessels from the thyriod arteries of the thyriod forms the part of the tumour, the teratoma in this region is called as 'teratoma of the thyriod'. And if the thyriod lobe could be identified separately from the tumour then is described as 'cervical teratoma' or simply 'cervical teratoma in the region of thyriod'(2). Considering the above criteria in our patient, the tumour could be titled as 'thyriod teratoma'. Furthermore, no left lobe of thyriod gland could be identified at the time of surgery and no thyriod tissue could be seen on histological examination. This could be interpreted as destruction of the lobe by the tumour. Since the tumours behave clinically similar ways and are treated by the same method, the division of this tumour into various terms is unwarranted and serves little purpose (1). Therefore, in the present patient we have titled the tumour simply as 'cervical teratoma'.

Cervical teratomas in the newborn were previously thought to be benign but recently malignant changes have been described (1,3). The diagnosis of malignancy depends upon undifferentiated tissue in the tumour. The other criteria are presence of tumour cells in the lymph nodes and distant metastases (3). In our patient, undifferentiated primitive tissue and mitotic figures in the tumour cells were clearly seen. Similary no distant metastases were detected. No recurrences have been noted if tumour is excised in the neonatal period (1). Since the patient was operated in this favourable period, prognosis can be considered as good.

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Acute Acalculous Cholecystitis By : S. Oranienbeg (A Case Report)

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Summary

S. typhi is considered to be au uncommon cause for acute acalculous cholecystitis in many regions of the world. 2 – 4% of adult patients with typhoid fever become chronic carriers and some of the carriers have no clear history of typhoid fever (3). Cholecystectogy is advocated as adjuvant to medical treatment for typhoid carriers (3). Nontyphoid salmonellae, are even more rare pathogens. S. oranienberg constitutes only 7.4% of the Nontyphoid salmonellae reported in carrier (7). Bonta and Lovinggood (1) reported one case of acute acalculous cholecystitis caused by S. oranienberg in a child. Main (6) reported one case caused by S. paratyphi, Craig and Mark (2) reported another case caused by S. indiana, and here we report another case of acalculous cholecystitis caused by S. oranienbeg.

CASE REPORT

A 32 year old Libyan female, house wife, was admitted to "7th April" Hospital, Benghazi on the 4th of August 1992, with 2 days history of moderate abdominal pain, nausea and repeated vomiting. The pain began in the right upper quadrant, grew progressively worse and radiated to the back and right shoulder. No change in the colour of stool. no diarrhoea and no fever were experienced.

Past history was significant for repeated attacks of similar complaints during the previous 20 years, with the frequency of one or two attacks per year. Tonsillectomy for chronic tonsillitis was done 18 years earlier and appendecetomy was performed for the same complaints 16 years earlier; without improvement in the patient's symptoms the patient was hospitalized 13 and 5 years earlier for the same pain and jaundice with subsequent improvement on conservative treatment (no availabe data). Family history was not suffestive.

On admission the physical examination revealed

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the patient to be afebrile, jaundiced, with tenderness in the right hypochondrial region (RHC) and a palpable spleen. Biochemical investigations were within normal limits apart from total bilirubin of 16.4mg% (Direct bilirubin was 12.0mg%), SGOT 60 u/l, SGPT 105 u/l, alkaline phosphate 182 u/l. Abdominal ultrasonography revealed dilated biliary tract with suspected stone at the distal end of CBD with markedly dilated gall bladder without stones, as well as an enlarged spleen.

Four days after admission, the patient's condition started to deteriorate. She became febrile (39.5 C), with marked pain in the RHC. The white cell count was 15.000 with neutrophilia, Serum amylase was 27 u/l. Total bilirubin was 6.2mg% (direct bilirubin 4.5%). The differential diagnosis of acute cholecystitis or acute cholangitis was considered. Parental Ampicillin, Gentamicin and Flagyl were started.

After 12 hours the patient's condition became worse and signs of pertionitis and septic shock were detected. Emergency surgery was performed.

On exploratory laparotomy, the gall bladder was found to be huge in size, flaccid, severely oedematous, with no stones or apparent perforation. The common bile duct (CBD) was dilated and congested. About 300 ml of thin yellow pus were aspirated from the peritoneal cavity mainly from the right paracolic gutter and pelvis. Exploration of CBD was performed, no stones were detected and T – tube drainge was instituted. T – tube cholangiography revealed no stones and free flow of the dye to the duodenum. Cholecystectomy was performed.

Samples of fluid from the gallbladder. CBD and the peritoneal cavity were sent for culture. Culture of the materials yielded S. oranienberg. Stool culture for Salimonella was positive. Post – operatively the dose of Ampicillin was increased to 8 gms/day with the addition of Chloramphenicol.

Patient had uneventful post – operative course, T – tube cholangiography done on the 9th post – operative day was normal. A sample of bile was taken before T – tube removal and the result was positive. The patient was discharged on the 11th post – operative day and monthly folow – up stool culture was advised.

CONCLUSION

Typhoid fever still exists in many places of the world and we should be alert to the associated gall bladder manifestations in the form of acute or subacute cholecystitis with or without cholelithiasis. The condition can have lethal complications such as perforation or gangrene. In this detailed case report, the patient developed septic peritonitis. In general acute acalculous cholecystitis is a potentially lethal disease and was found to be associated with a higher mortality rate, more than twice that of acute calculous cholecystitis (5).

Acute acalculous cholecystitis caused by Salmonella spcies can be easily overlooked if bacteriologic studies are not carried out at the time of operation especially if the patient is a chronic typhoid carrier without a clear history of typhoid fever. One might expect 80 – 85% cure rate after cholecystectomy (4), and a 95% cure rate from cholecystectomy combined with simultaneous antibiotic administration (3, 8).

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Giant Pseudocyst of the Adrenal Gland
Report of Two Cases and Review of Literature

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SUMMARY

Two cases of giant cysts of the Adrenal gland in female patients have been reported, emphasis on the rarity of adrenal cysts as clinical and pathological entities have been highlightened. Despite the large size of the cysts, minimal to moderate pressure symptoms were encountered.

Although a mild degree of hypertension was discovered in one of the cases preoperatively, no disturbance in adrenal functions was noted. The cysts were surgically removed successfully.

The relevant literature is briefly reviewed.

الملخص

هذا تقرير طبي عن حالتين من الكيسات الضخمة في الغدة الكظرية لدى امرأتين. ورغم ضخامة الكيسة في كل حالة إلا أنه لم يلاحظ لها تأثير ضغطي كبير ولم تلاحظ أي اضطرابات في وظيفة الغدة الكظرية في المريضتين. وتم استئصال الكيسة بدون مضاعفات.

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INTRODUCTION

Adrenal cysts are rare lesions which are encountered incidentally, the vast majority are minute in size, unilateral and found by greiselius in 1670 (Doran) (3). Foster in 1966 reviewed the World literature and collected 220 cases (4). In 1977 Mnaymneh et al reported 6 cases increasing the number of the total reported cases to 256 all over the world (5). This report adds two more cases of giant adrenal pseudocyst to the world literature.

CASE 1:

A 24 year old, Libyan female referred 7 days after normal delivery, complaining of swelling and heaviness in the left side of the abdomen since the beginning of the third trimester of her pregnancy and a mild degree of hypertension that was detected by her attending clinician that returned back to normal level after delivery. She is a mother of two other healthy children. There was no history of jaundice or trauma. Clinical examination revealed a healthy obese female (95.Kg) with no pallor or jaundice, blood pressure was 140/90mm Hg. The abdominal examination revealed a huge, smooth intra – abdominal oval mass about 20×15 cms in diameter, tense slightly tender; its medial and inferior borders were well defined and the other two borders were merging deeply under the left costal margin. There was no hepato – splenomegaly or evidence of free fluid in the peritoneal cavity.

Haematological, as well as biochemical investigations including VMA and HVA levels were within normal limits. Urine examination was normal. Casoni intradermal test was negative. Plain x – ray abdomen showed a vague soft tissue mass in the left upper part of the abdomen with fine rim of calcification Ultrasonography and CAT scanning of the abdomen revealed the lesion to be cystic, displacing the spleen anteriorly and the left kidney downwards. A provisional diagnosis of left suprarenal cyst was made. Angiography and radio isotope studies were not carried out.

Laparotomy was then performed through a trans – abdominal approach, a tense cyst was found situated in the region of the left adrenal gland. Five liters of reddish – brown clearfluid were aspirated. The wall of the cyst was thick without any macroscopic evidence of malignant degeneration. The cyst was totally excised. The post – operative course was uneventful, the patient being discharged on the 10th post – operative day and remained asymptomatic during the last 15 months of follow – up. Histopathological study revealed the cyst wall to be made of dense fibrous tissue with no epithelial lining, with areas of calcification and micro – haemorrhages, small columns of cells of adrenal tissue were also seen caught up in the fibrous wall of the cyst. The diagnosis of pseudocyst of the adrenal gland was confirmed.

CASE 2:

A 25 years old, Libyan female complained of gradual abdominal distension and heaviness in the left loin over the past 3 years. She is a mother of two healthy children. The result of general examination was normal. Abdominal examination revealed the presence of painless smooth cystic mass fixed in the left upper quadrant.

Haematological and biochemical investigations were within normal limits. Casoni intradermal test was negative. Plain x – ray of the abdomen showed no calcification. Ultrasonography & CAT scanning of the abdomen revealed a well defined cyst displacing the spleen upwards and the left kidney downwards.

At laparotomy, the cyst was found to contain 6 liters of reddish – brown clear fluid, the cyst was totally excised and the patient was discharged on the 9th post – operative day. Over 11 months of follow – up there was no evidence of adrenal insufficiency, and the patient remained asymptomatic.

The histopatholgical examination showed that the cyst wall consisted of fibrous tissue that was devoid of any epithelial lining or calcification, scattered islands of adrenal tissue was also identified and diagnosis of pseudocyst of the left adrenal gland was confirmed.

DISCUSSION

Adrenal cysts are rare lesions forming an incidence of 0.06% at autopsy (Wahl) (13) and the correct diagnosis is seldom made before operation or necropsy. There is equal frequency of occurence on right and left sides, bilateral adrenal cysts are more common in females (7,9), at a rate of 2:1. They have been reported in all age groups, with peak incidence between the third and fifth decades (7). Pseudocyst of the adrenal gland seems to have a tendency to appear during the immediate post – partum period (4, 9). This seems to be the case in our first patient.

The aetiology and pathogensis of adrenal cysts are not well understood but a haemorrhagic cyst can occur in the fast growing adrenal tumours.

Based on histopathological characteristics, adrenal cysts have been classified into four types; Parasitic 7%, Epithelial 9%, Endothelial 45% and Pseudocysts 32% (1).

Since hydatid disease is endemic in Libyan Arab Jamahiriya, the possibility of Echinococcosis was ruled out in our Patients on the basis of negative serologic tests and ultrasonographic features.

Although pseudocysts are generally small to moderate in size but they may attain a huge size. This is possibly due to the expansion of the cyst in a potentially accomodative retroperitoneal space. The cyst we removed from our two patients was enormous in size containing five and six liters of fluid, Rampina (11) reported on a voluminous cyst containing 11 liters of fluid.

Pseudocysts usually contain dark brownish fluid. This is said to occur as a result of haemorrhage in a normal or pathological gland, this has been reported in conjunction with birth trauma and haemorrhageic disease of the new born. Adrenal haemorrhage can also occur as result of trauma, burns shock and toxaemia of pregnancy.

Because of their location, they rarely cause symptoms in the early stage and only on reaching big size they cause mild discomfort to the patient. This was the case in our second patient that remained symptom free a long time before presentation.

Adrenal cysts usually don't affect the adrenal function and the transient hypertension that was encountered in our first patient could be related either to the pregancy or to the mechanical effect of the cyst causing renal ischaemia with release of pressor substances (8).

Histologically the cyst wall is usually fibrous without epithelial lining, the presence of islets of adrenal tissue with calcification in the cyst wall usually characteristic of pseudocyst (10). In our first case a rim of calcification was seen, but absent in the second case. In both specimens no definite evidence of underlying pathology in the adrenal gland tissue was detected. Therefore, we can assume that in these patients, the pseudo cysts were found as a result of spontaneous haemorrhage in otherwise normal adrenal gland.

CONCLUSION

Pseudocysts of the adrenal gland are rare and bengin lesions. Awareness of the condition with the aid of the modern imaging techniques should render diagnosis relatively easy. Surgical exicision is curative.

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Aniridia
(A Case Report)

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SUMMARY

A family of six members; father, mother and four male children are reported to have complete aniridia with other ocular maldevelopment but no systemic involvement. All male members of the Family are affected, but the female (mother) is Free of any involvement. Repeated genetic study is non – conclusive Details of exact pedigree is not available. Imunological survey reveals low levels of IgG and IgA. The recent birth in the same family is a male child with all the ocular mal development seen in the other children.

الملخص

وجد في عائلة مكونة من ستة أفراد، أن القزحية غائبة تماماً في الوالد وأطفاله الأربعة الذكور.. وإلى جانب ذلك كانت هناك تشوهات خلقية أخرى في العين، وإن لو يوجد فيهم أي تأثير جسمي عام. أما الأم فلم يلاحظ عليها أي إضافة.

إن تكرار الدراسات الوراثية، لم يظهر شيئاً مؤكداً، أما الفحص المناعي فقد أظهر تدنياً في مستوى الغلوبين المناعي الجيمي والألفي، ونقدم في هذه الورقة دراستنا عن هذه العائلة.

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INTRODUCTION:

Congenital malformations are the scars of foetal and embryonic disease. Congenital anomalies are divided classically into environmental and hereditary. Aniridia can be sporadic or hereditary, as autosomal dominant with a peneterance of about 85 – 90%. Aplasia of macula is the most common association showing the failure of ectodermal development at 11 – 12th week of embryonic life when ectodermal layers of the iris and fovea become differentiated. Aniridia is a major blinding affection in which the iris is rudimentary, iris can be appreciated on gonioscopy (4). The anomaly is nearly always bilateral and also frequently associated with additional ocular malformation and also systemic disease, like Wilm's Tumor (2), Buphthalmos, and other maldevelopments in angle, seen in nearly 50% of cases and Nystagmus and cataract seen in 80% of cases (5).

CASE REPORT

A Libyan family, resident in Benghazi was the subject of this study. It consisted of the father (38 yrs), his wife (28 yrs) and four male children aged 6 1/2, 5 1/2, 3 1/2 and 2 years. All members had a detailed ocular and systemic examination. A paediatrician examined all the children. There was nothing significant in maternal history and no history of consanguinity. The mother was absolutely normal. Father had marked dimunition of visual acuuity PL. only, possibly since early childhood. The examination of father revealed complete corneal opacity of leucoma nature, which made further examinations of the eye not possible, and a high intra – ocular pressure, these all could be due to aniridis. Table (1) shows the details of various examinations made on members of this family. It shows that two older children, aged 6 1/2 and 1/2 years, are more affected in the acuity and other lesions, like raised intra – ocular pressure and lenticular changes.

These changes in ocular media made the fundus details obscure. In the other two younger children, aged 3 1/2 and 2 years, the affection was of mild nature with better visual acuity and less lenticular ohanges, but with poorly controlled intra – ocular pressure. The fundus examination of these two younger children revealed pale optic discs, possibly the cause of cause of the low acuity of vision. Nystagmus and cataract were present in all children but there was no systemic involvement. The gonioscopic examination (ERG) could be done. A genetic and immunological survey was also performed, for members of the family, and the results are shown in Table (2).

DISCUSSION

Classification of aniridia includes. I. Autosomal dominant. II. Autosomal Recessive, III. Sporadic cases and IV. With systemic diseases. Autosomal dominant aniridia with other ocular pathology has been well documented (3). Aniridia must be differentiated from other autosomal dominant disorders, such as coloboma of Iris, choroid, and anterior cleavage syndromes. The present cases described are aniridia with ocular pathology only, without any specific genetic inheritance, inspite of repeated genetic study, although all family members had bilateral symmetrical involvement for visual acuity and high intra – ocular pressure, conventional treatment did not help. In the present study, a significant finding was the low levels of IgG and IgA in three affected children as well as the father. IgG is the most common immunoglobulin in blood, and is responsible for humoral immunity against bacterial and viral infections. IgA occurs in plasma and also in tears and other seromucus secretions, where it plays an important role in maintaining local immunity. The low levels of IgG and IgA suggest a decrease in the humoral protective mechanism (1). The exact significance of such finding in these is interesting and needs more evaluation.

Table (1) : Details of ocular examinations made

S. No.	Case	V.Acuity RE	V.Acuity LE	Iris	Lens	IOP	Fundus	Nyst	Squint
1.	Father	PL	PL	Not seen	Not seen	NAD	Not seen		
2.	Mother	6/9	6/9	NAD	NAD	NAD			
3.	Child 6 1/2	1/60	1/60	Aniridia	Cat.	High	Not seen		
4.	Child 5 1/2	1/60	1/60						
5.	Child 3 1/2	4/60	4/60				Disc Pale		
6.	Child 2	4/60	4/60						

Note: Fundus Examination by INDIRECT METHOD. Gonioscopy and ERG not done.

Table (2): Levels of Immunoglobulin and Complement (C&C) in Cases Studied

S. No.	Case	Hb%	Immunoglobulin mg/L IgG *(800 – 1600)	IgA *(140 – 400)	IgM *(20 – 200)	Complement C3	C4	T. Cell
1.	Father	16.4	992.1	84.6	72.7	137	44	65%
2.	Mother	15.0	885.5	256.3	136	157	33	62%
3.	Child 6 1/2	12.1	531.6	46.9	72.7	111.8	46.8	68%
4.	Child 5 1/2	10.1	531.6	76.7	60.6	66.6	31.5	55%
5.	Child 3 1/2**	–	–	–	–	–	–	–
6.	Child 2	14.5	457.6	69.9	99.3	99.9	10.8	58%

* Normal levels

** Could not be done

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Arnold - Chiari Malformation (A Case Report)

H. Ali and S. Zunni

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SUMMARY

Arnold – Chiari malformation is a congenital anomaly of the hindbrain. It is a rare congenital malformation of unknown causes. Though initial cases were reported among the European population, no race seems to be spared and there have been occasional case reports from all the world. Males and females are equally affected. A case recently seen by us is being reported.

الملخص

تصف هذه المقالة مريضاً مصاب بالتشوه الخلقي في الدماغ المؤخّر (آرنولد ـــ كاياري). وهو تشوه خلقي نادر الحدوث لا يعرف لظهوره سبب، ورغم أن الحالات الأولى وجدت عند الأوروبيين، إلا أن جميع الأجناس، وبدون فروق بين الذكور والإناث، معرضون للإصابة به كما تدل التقارير الواردة من جميع أنحاء العالم.

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CASE REPORT:

A 60 year male was admitted to the "7th of April" Hospital, Benghazi in February 1992 complaining of unsteadiness during walking (but able to walk with the aid of a stick), heavyness of the right side of the body, and loss of sensation on the right lower extremity and right radial part of arm and hand. The neurological history showed that since childhood he had a problem with walking, never able to run, to jump, or to walk in a straight line. His condition had deteriorated and on 9th October, 1984, he was operated upon in london for posterior fossa decompression with laminectomy from C1 to C3.

After operation, there was marked deterioration of his condition, resulting first in tetraplegia, then with right side hempilegia. Physiotherapy was recommended but there was heaviness of right side with impairement of sensation and unsteady gate and equilibrium. Physical examination: the patient was conscious and alert, a short neck, scar in the cervical and occipital area – was noticed but no neck stiffness. Neurological examination showed mild dysarthria and nasal speech.

I. Cranial nerve: Anosmia right nostril.

II. Cranial nerve: Optic disc and visual field normal.

III, IV, VI. Cranial nerves: Pupil equal, central, circular and reactive to light, external occular movement normal. Nystagmus with an oblique rapid motion down and to the left in all positions, and 3rd degree nystagmus with downbeat component. Other cranial nerves normal. Motor system examination showed minimal weakness of right upper and lower extremities when the arms are out – stretched. There was mild ataxia in Nose – Finger test, more on right side, patient not able to do fine finger movement. There was gross ataxia of head – knee – shin test.

Sensory system examination showed blunting of pin prick touch on left side, decreased vibration sense on right side, and absent position sense on right lower extremity.

Gait examination: Walks on wide base, slightly unsteadily, only with support of stick or crutches. Rombergs sign postive with feet together.

Investigations: X – ray cervical spine (fifure. 1) showed that there is sizeable sub – occipital defect with **tantaullium** clips in the upper most part of the spinal canal, the spines and laminas of C2 and C3 appear to have been removed, and probably also the posterior of the atlas. There is kyphosis at the C2 and C3 level.

X – ray of the skull (Figure 2). showed that a posterior fossa decompression has been performed and the bone edges look healthy. The remainder of the skull showed no abnormality. CT scan of brain (figures 3 and 4) showed no abnormality. CT scan of Skull (figure 5) showed defect in the base of bone of the skull. A diagnosis of Arnold – Chiari malformation after posterior fossa decompression, was made.

DISCUSSION

Arnold – Chiari malformation is a congenital anomaly of the hindbrain. There is displacement of the cerebellar tonsils and of an elongated medulla oblongata downwards into the cervical spinal canal. The malformation prevents the agress of CSF from the fourth ventricle into the subarachnoid space. It is sometimes associated with lumbosarcal spinabifida and with meningocele or meningomyelocele. Chiari in 1891, described in great detail the many features of this malformation in infants, children and adults.

Mac Farlane and Maloney (6) in 1957 have observed congenital narrowing of the cerebral aqueduct sufficient to cause hydrocephalus in half of 20 cases of Arnold – Chiari malformation. Gardner (1965) (4) has suggested that a Chiari malformation, or less often the Dandy – Walker syndrome, may result in dilatation of the central canal of the spinal cord early in life (hydromyelia) and that this, in turn, is the commonest mechanism by means of which syringomylia is produced. The observations of Appleby et al (1968) (2) and Barnett et al (1974) (3) give some support to this view.

The etiology of Arnold – Chiari malformation is still unknown. The Arnold – Chiari

malformation may be produced in animals by excess vitamin – A, arsenate, or clofibrate (Marina Padilla, 1980 & 1981) (7,8).

There are characteristic symptoms to assist in the diagnosis of this syndrome. According to Joseph W. Spooner et al (1981) (9) there is headache, ataxia, dysphagia, weakness, oscillopsia, diplopia, and blurred vision with vertical nystagmus, progressive upper limb paralysis, and sensory loss (Gol and Hellbusch, 1978) (5).

In our patient, the present neurological picture is complicated and consists of a combination of pyramidal signs, cerebellar signs: ataxia, nystagmus and posterior column defects.

Diagnosis of Arnold – Chiari malformation depends on X 2ray of Skull. Metrizamid myelography performed with the patient supine was, until recently, the most reliable means for diagnosis. The cerebellar tissue and cervical cord obstruct an upward flow of metrizamid and give a characteristic picture.

CT scanning may be combined with myelography to show the extent of the Arnold – Chiari malformation or basilar invagination and dilatation of the cervical cord.

Magnetic Resonance Imaging (N.M.R.) techniques dramatically improves both anatomical resolution and tissue characterization information. In our patient, the diagnosis of Arnold – Chiari malformation, was confirmed by CT scanning and X – ray of the skull.

The treatment of Arnold – Chiari malformation is far from satisfactory. If clinical progression is slight or uncertain it is probably better to wait. If progression is certain and disability is increasing, upper cervical laminectomy and enlargement of the foramen Magnum are indicated, Often this procedure halts the progress of the illness, bnt it must be done cautiously.

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تعليمات للمؤلفين:

1 ـ ترسل الأبحاث إلى رئيس هيئة تحرير مجلة قاريونس الطبية ص . ب . 18251 بنغازي — الجماهيرية العربية الليبية الشعبية الاشتراكية العظمى .

2 ـ يشترط لقبول البحث عدم سبق نشره أو الاتفاق (الارتباط) على نشره في أي مكان آخر، كما لا يجوز اعادة ما ينشر في هذه المجلة الا بإذن من هيئة التحرير.

3 ـ تقبل الابحاث من اي مؤلف في اية دولة .

4 ـ تقدم المقالة (البحث) من نسختين مطبوعين على الآلة الكاتبة، باللغة الانجليزية مع ترك مسافتين بين السطر والآخر ومكتوبة على ورق ابيض، خالية من الأخطاء، مختصرة ومنسقة الاسلوب . كما يختار لها عنوان مختصر كرأس للموضوع ويستعمل في فهرست المواضيع مع بيان المصطلحات الواردة في البحث، ويكتب ذلك على ورقة مستقلة كصفحة أولى للمقال، كما يحرر عنوان البحث على الورقة الثانية، اما الورقة الثالثة فيطبع عليها اسم المؤلف او المؤلفين والجهة التي يتبعونها . وتتضمن الورقة الرابعة تقديم لموضوع البحث الأساسي . وعلى العموم يقدم المقال بالصورة التالية : ملخص ـ تحليل ومناقشة لجوانب البحث ـ التعريف ـ المراجع .

5 ـ يفضل تقديم ترجمة عربية لملخص البحث وكذلك للعنوان واسم المؤلف والجهة التي ينتمي اليها وذلك في ورقة منفصلة في آخر المقال .

6 ـ الجداول والرسوم البيانية والتوضيحية ينبغي أن تطبع كل واحدة منها على ورقة مستقلة مع وضع عناوين لشرح المضمون ويعرف به دون حاجة للرجوع الى الملاحق كما يشار الى اماكن المثبتات .

7 ـ ترجمة مراجع المقالة وتنظم أبجدياً بأسماء المؤلفين وتكتب تأثيث المراجع بالرقم وعلى سبيل المثال :

1 ـ براي ـ ج . ي (1930) ـ عامل الوراثة في مرض الربو وأمراض الحساسية الاخرى ـ مجلة برت الطبية : 384:1

2 ـ دفاس ـ ج . م . ، تالانستال ـ م . إ . ، ودوندي ـ ج . و. (1974) تقييم العقاقير المضادة للروماتيزم ـ لانست (المبضع) 214:39

3 ـ سوبل ج . ر. (1960) ـ استئصال اللوزتين في الطفل المريض بالحساسية عن بريجال ـ س . عوامل الحساسية الحديثة ـ دار ماكجروهل المتحدة للكتاب ـ نيويورك .

8 ـ ترسل 25 نسخة من المقال المنشور الى المؤلف، ويتكفل بدفع قيمة ما يزيد على ذلك، كما ترسل النسخة الأصلية عند إعادة الطبع .

9 ـ للاستعلام بخصوص نشر الأبحاث والاعلانات والاشتراكات تكون المراسلات باسم رئيس التحرير.

مجلـــــة
قـاريونـــس الطبيـــة

المجلة الرسمية لجامعة العرب الطبية

ص . ب : 18251 بنغـــازي

الجماهيرية العربية الليبية الشعبية الاشتراكية العظمى

مجلة قاريونس الطبية نصف سنوية وتتناول العلوم الطبية . مجلد يحوي عددين احدهما في يناير والآخر في يوليو

السعر	العملة المحلية	العملة الأجنبية مع رسوم البريد
اشتراك سنوي	4 دينار ليبي	12 دولار
نسخة واحدة	2 دينار ليبي	6 دولار
50 مستخلص من البحث	5 دينار ليبي	15 دولار

تنبيـــه :

- لا تمثل المقالات التي تنشر في هذه المجلـة وجهـة نظر الكلية ولا هيئـة التحرير ويعتبر الكاتب وحده المسـئول عمـا فيهـا من آراء وعن صحة ماجاء في هذه المقـالات .
- يرجى من الكـاتب قراءة التعليمات والإرشـادات المطبوعة في الصفحة التالية وينصح الراغبين في نشـر إنتاجهم بقراءة الإرشادات المطبوعة خلف هذه الصفحة والتقيد بها .