MEDIKKA

THE INTERNATIONAL JOURNAL OF THE UNIVERSITY OF NIGERIA MEDICAL STUDENTS

- CAREER PROSPECTS OF MEDICAL STUDENTS
- THE THREAT OF HCV
- TETANUS
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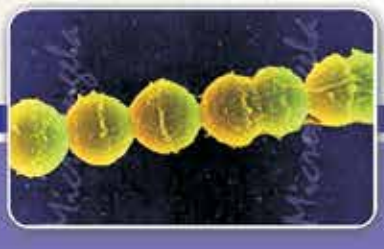
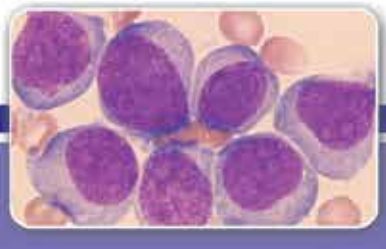
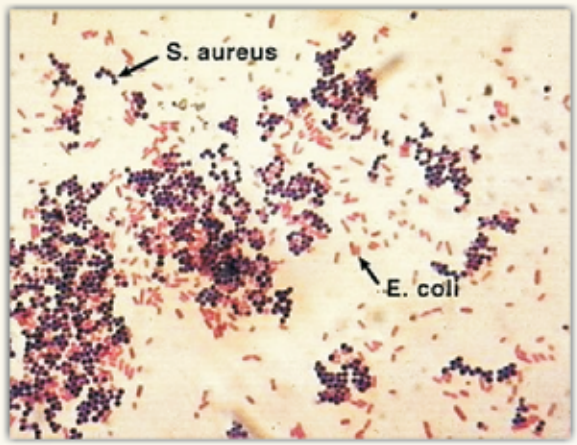




The UTI article

ABSTRACT

This is a retrospective study carried out in patients who presented to the UNTH Enugu, microbiology laboratory within the period of 1st April, 2004 31st March 2005 with the diagnosis of UTI. UTI was defined by the clinical evidence of dysuria, frequency, urgency, and/or haematuria, and/or pyuria, and/or flank pain. Study was targeted at isolating the common organisms responsible for UTI in this environment as well as depicting the susceptibility of these urinary pathogens to commonly prescribed antibiotics. This is aimed at illustrating the current trend of rapidly evolving/emerging bacterial resistance to easily obtainable and affordable antibiotics with less risks which leaves the clinician with no other option but to prescribe the newer, less available drugs with its attendant harm. Subjects that had laboratory evidence of UTI were chosen, which is defined as growth of = 10^5 cells/ml of neat urine collected properly in the standard 'clean catch midstream' method.
Growth was on the Mueller- Hinton agar and sensitivity was done by the standard disc diffusion technique. Results gathered implicated the following organisms... and peak resistance was to...and sensitivity to... E. coli was most common...Resistance to Amoxicillin, ciprofloxacin... Health concerns...Increased cost...MDR



UTIs are the commonest infectious disease(EHINMIDU) as they are responsible for hospital visits made by 50,000/million persons per year. In the pediatric age group they are the commonest causes of febrile convulsions(AZUBIKE). every female has a 20% life time risk of coming down with a UTI(David Howes) In our environment in which most available antibiotics can be obtained 'over the counter', bacterial resistance is a natural sequelae thus it becomes imperative that a study aimed at identifying exactly who is winning the tussle of microbes versus anti microbes be conducted. The microbes are ever evolving and in the case of UTI this has resulted in increasing cases of relapse of disease after treatment. UTI patients commonly presents early to the out patient clinic due to its discomforting nature. Mostly implicated are fecal organisms sourced from patients own intestinal flora: E. coli, S. aureus, Klebsiella, Proteus, S. epidermidis(in sexually active young women) which commonly spread to the urinary tract via the ascending transurethral route. Treatment by oral antibiotics is usually effective, initially amoxicillin, trimethroprim sulphamethoxazole which seem less effective these days and have the cephalosporins, flouroquinolones and nitrofurantoin taking over. The focus of the study is to depict the rising profile of bacterial resistance to commonly prescribed urinary antibiotics as well as bring to light the "new kids on the block"

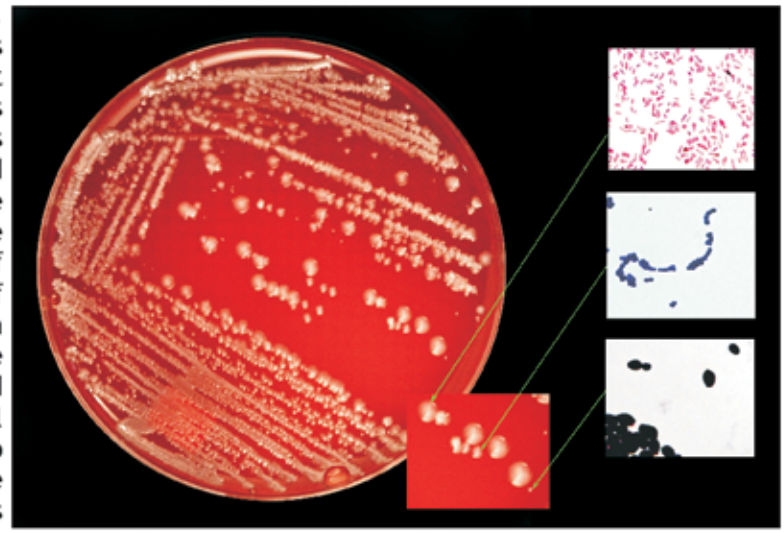
LITERATURE REVIEW

UTIs are wont to occur in an individual's lifetime however being female, pregnant or having an inherent renal pathology(e.g. vesicoureteric reflux, obstructions e.g. presence of posterior urethral valve, congenital anomalies e.g. bifid ureters) increases the chances greatly. The disease has a peculiar age and sex incidence(David Howes,,MD) and no racial difference in incidence pattern. In the neonatal period, it is more common in males as part of a gram negative sepsis syndrome and 5-10 times more in uncircumcised males. In preschool kids the incidence of disease is 2% with girls being 10 times more at risk than boys, thus it is rare in pre school males. It is also more common in young and middle aged women and at this age , clinical evidence of a UTI in male portends presence of a previously undetected pathology of the urogenital system e.g. bifid ureters, PUJ obstruction or bladder outlet obstruction due to a hyperplastic prostate. Frequently implicated organisms are the organisms of the intestinal flora leading the pack of which is E. coli, S. aureus. S. fecalis, Klebsiella, Pseudomonas. Spread to the urinary tract is achieved commonly via the ascending transurethral route and less commonly hematogenous, lymphatic or direct spread through communicating fistulae. Establishment of infection is an interplay between the virulence of the organism(possession of flagellae, adhesions) and the host's defence mechanism(complement, neutrophils, commensal bacteria, voiding, uroepithelium). Treatment is aimed at cure though relapses(i.e.

reappearance of the same organism within 7 days of completion of anti microbial treatment) are known to occur and when they do, makes a case for a functional or anatomical predisposing factor. Patient is started on broad spectrum antibiotics whilst definitive laboratory evidence of infection is awaited. Positive bacteriuria for UTI is defined as

≥10^2 coliforms/ml neat urine + pyuria in females
OR
≥ 10^5 cells/ml in females
OR
≥ 10^3 cells/ml in males
in a properly collected clean catch mid stream urine put in the right container and sent to the laboratory in good time
OR
presence of any growth in a urine sample obtained by suprapubic aspiration.

Definitive treatment depends on bacterial isolates from culture and susceptibility profile of isolates in a simple UTI (i.e. UTI occurring in a non pregnant female with normal renal anatomy or male neonate) can be treated with amoxicillin 250mg twice daily for 3-5 days or trimethoprim 200mg twice daily for 5days and in neonates cotrimoxazole 7mg/kg/day for 10days. However this treatment protocol is more or less obsolete and historical due to the emergence of MDR strains of bacteria which have established substantial resistance to the above drugs. This makes the case for the involvement of ever antibiotic regimen in the treatment of UTI, involving antibiotics such as- Ciprofloxacin, Gentamicin - however, due to its unique mechanism of action, Nitrofurantoin which has been in use against UTIs is still effective, as resistance to it has not been achieved by the commonly implicated organisms except Pseudomonas and Proteus.



Research findings from different quarters seem to correlate these features. E.g. in the July 1995 study in The Seychelles' Victoria Hospital E.coli isolates from urine samples of UTI patients shows a 78.6% resistance against Ampicillin, Amoxicillin and a 54.8% resistance against Cotrimoxazole (Septrin). Same E.coli isolates showed a 75% susceptibility to Gentamicin, Nalidixic acid and Nitrofurantoin. Also, Proteus specie isolated in same study showed a 100% resistance to Nitrofurantoin but were susceptible to Ampicillin, Septrin, Gentamicin, Nalidixic acid. Klebsiella spp. specie were resistant to Ampicillin, Cotrimoxazole but susceptible to Gentamicin, Nitrofurantoin, Nalidixic acid. Pseudomonas specie were susceptible to only Gentamicin and Azlocillin. In a similar study conducted by The Kathmandu Medical college, Kathmandu valley, Nepal in 2005; E.coli was the most prevalent organism isolated(at 49%) and it showed a 100% susceptibility to Nitrofurantoin and resistance to amoxicillin and ciprofloxacin. S. aureus was 88.8% susceptible to 2nd generation cephalosporin and 77.7% susceptible to

ATB	E.coli	S.aureus	P. aeruginosa
Ciprofloxacin	93.75	97.06	95.35
Amoxycillin	6.25	6.98	5.88
Gentamizin	78.69	91.18	86.05
Ampicillin	50.00	17.65	60.46
Penicillin	0.00	0.00	0.00
Tetracycline	31.25	29.41	32.56

He noted that the highest incidence of resistance was seen in samples collected from students of the Faculty at ABU and commercial sex workers. These two groups are also associated with gross antibiotic use thus fostering the bacterial resistance noted their samples. The study was carried out on Zaria residents with subjects including students of the Faculty of Pharmaceutical Sciences, ABU, Zaria and Kaduna State Polytechnic Zaria, illiterate men and women and commercial sex workers. Samples from the illiterate people showed the least resistance.

From the above results, we can rightly infer that certain antibiotics have lost their efficacy in treating UTIs to emerging bacterial resistance and this seems to be a global trend. Also the emerging resistance directly correlates with wanton antibiotic use(abuse) as seen in the Ehimmadu study. However, amidst growing resistance, Nitrofurantoin still has most of bacterial isolates(except Pseudomonas and Proteus) sensitive to it and based on its mechanism of action it is likely to be impervious to neo-resistance. It is a fairly safe drug whose only indication is UTI (urinary antiseptic) and can be used in simple UTI's and chronic UTIs(due to a junctional renal pathology). It is however contraindicated in renal insufficiency, infants less than 3 months old and patients with G6PD deficiency and nursing mothers breast feeding such infants.

Materials and Methods

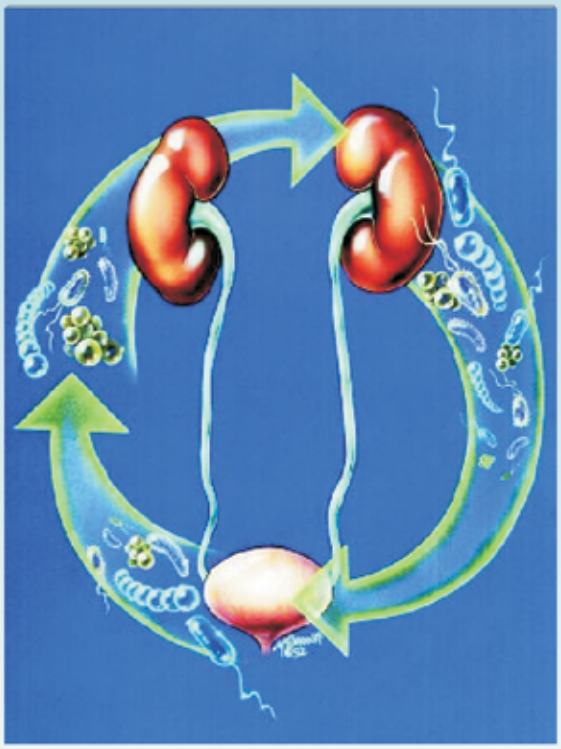
A total of 1814 subjects were used for the study. Subjects were chosen who had significant bacteriuria in their urine sample(in addition to clinical symptoms of UTI) who presented to UNTH Enugu Microbiology department in the period of 1st April 2004- 31st March 2005. Positive growth was defined as growth of =10^5 organisms per ml neat urine or = 10^2 coliforms/ml neat urine + pyuria or growth of any organism in a urine sample obtained by a suprapubic tap. Urine samples from a total of...patients were used;...females and...males. Peak age incidence/male and female, mean age range...

Each sample was inoculated in triplicats into MacConkey agar. Media used mannitol salt agar, MacConkey agar, Nutrient, Muellar Hinton agar.

Inoculated media was incubated aerobically at 37°C for 18 24 hours. Characteristic bacterial isolates were aseptically isolated and subjected to microscopical and appropriate biochemical tests for proper identification.

Antibiotic susceptibility test of isolates to commonly prescribed antibiotics was done according to standard microbiological procedure. The antibiotic discs used were those of Gentamicin 10ug

Amoxicillin	30ug
Ampicillin	10ug
Amikacin	10ug
Tetracycline	30ug
Ciprofloxacin	5ug
Spectinomycin	100ug
Cotrimoxazole	25ug
?nitro	
Nalidixic acid	13ug
Cefotaxime	30ug
Amoxyclav	30ug



Norfloxacin	10mg
Ceftazidime	30ug
Cefoperazone	75mg

They were studied overnight and the resulting culture was used to seed the melted Muellar Hinton agar at 45oC and poured into sterilized plates aseptically. They were allowed to stand for 18hours after which bacterial isolates were counted according to the ??Miles and Misra method to calculate the degree of bacteriuria/ml of neat urine sample.

CAREER PROSPECTS OF MEDICAL STUDENTS AT THE UNIVERSITY OF NIGERIA ENUGU CAMPUS.

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SUMMARY

In this pilot survey, 132 fifth year medical students were interviewed to find out their career prospects after graduation from the medical school. The male to female ratio was 1.4: 1 and 77.3% of the students were between the ages of 20 25 years. 89.4% plan to practice medicine, and 90.9% of this group plan to do postgraduate specialist courses. 50.8% of the medical students plan to migrate to other countries after qualification.

KEY WORDS Career, Medicine, Migration

INTRODUCTION

The career structure of medical students is different from that of other disciplines. Most of the time, their career follows a stereotype pattern. Whereas those in other disciplines look for jobs upon graduation and youth service, the medical doctors have the option of either working as general practitioners or going through a rigorous residency programme to become specialists.

The trend for some years now is for Nigerian medical doctors to migrate to developed countries in search of 'greener pastures'. As the economic situation in the country dwindles, more and more doctors leave the country each year. A report by the United Nations Development Programme (UNDP) in 1993 estimated that 21,000 doctors left Nigeria for the United States[1].

The aim of this study is to assess the future plans of a given number of medical students with regard to their future practice of medicine and migration to other countries.

MATERIALS AND METHOD

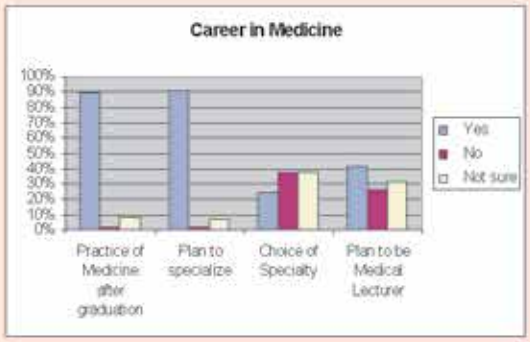
Questionnaires were distributed to 150 students of the 2006 class of the College of Medicine, University of Nigeria, Enugu Campus (UNEC) but 132 (88%) of them returned the completed questionnaires. Analysis was made regarding their age, sex, marital status, career options and desire to migrate to other countries.

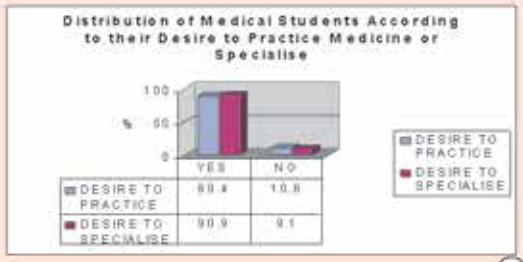
RESULTS

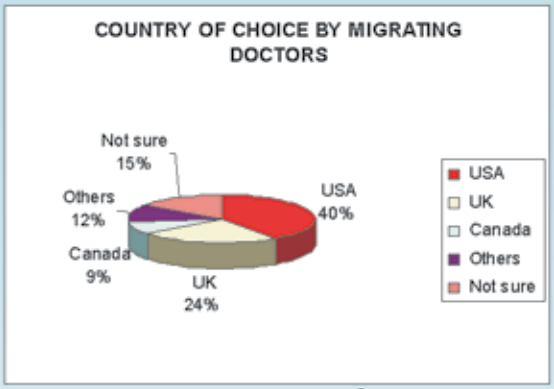
The results of this investigation are illustrated below:

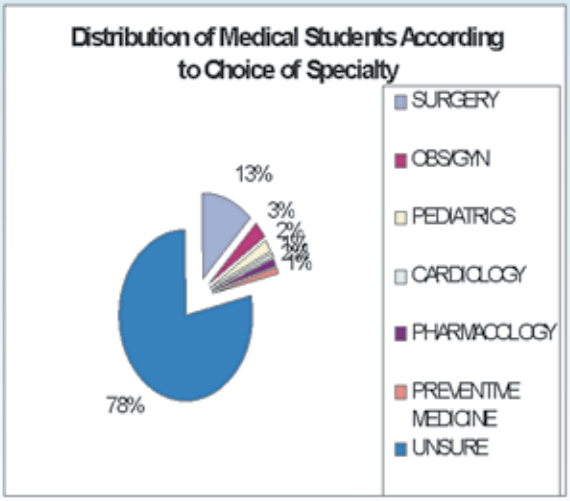
Table 1: DEMOGRAPHIC VARIABLES

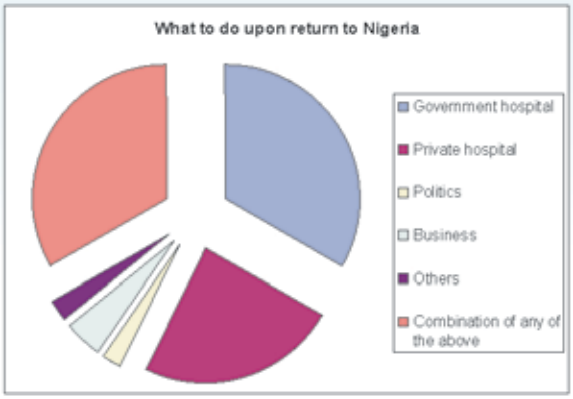
	Number	Percentage
SEX:		
Male	78	59.1%
Female	54	40.9%
AGE:		
20-25 years	102	77.3%
26-30 years	29	21.9%
31-35 years	1	0.8%
MARITAL STATUS:		
Single	121	91.7%
Engaged	8	6.0%
Married	3	2.3%

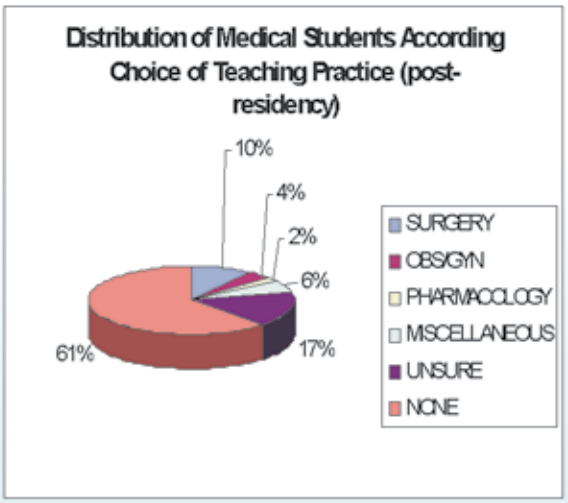


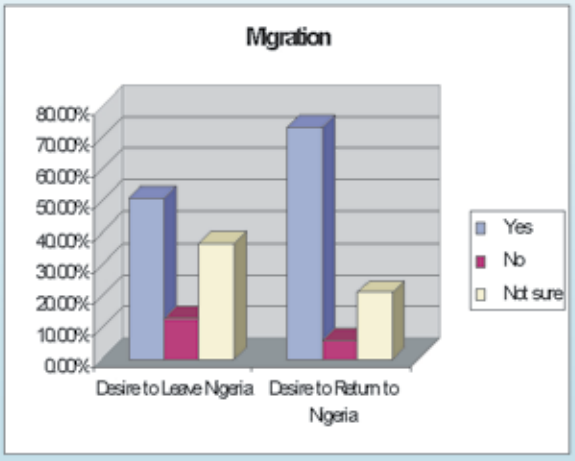












DISCUSSION

The medical students of the 2006 class, College of Medicine UNEC, are academically minded and intend to achieve the highest goals in their medical career. While most medical students will eventually become practicing doctors, few will become medical lecturers. As undergraduates, most students are not sure of their future area of specialization. This study indicates that the trend of migration of doctors to developed countries especially to USA will continue. The United Kingdom is also popular but with recent measures put in place by the UK government it is now difficult for migrating doctors to get jobs. Other countries in Europe are options. However, this '*brain drain*' in Nigeria is not primarily the fault of the doctors. A high percentage of those who would migrate, wished to return and work in Nigeria. The problem is perpetuated by the deteriorating economic situation in the country. Medical doctors who migrated in the past had the good intention of returning to

Nigeria but were faced with the reality of the unfavourable political and economic climate which hampers infractural development in hospitals; thus they decided to remain where they were sure of "increased income, greater access to enhanced technology, an atmosphere of general security and stability, and improved prospects for one's children".[2]

The statistical significance of this pilot survey will be determined following a more detailed study using a larger population and appropriate statistical sampling frame.

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ARTEMISININ COMBINATION THERAPY AND TREATMENT OF MALARIA IN CHILDREN AT THE UNIVERSITY OF NIGERIA TEACHING HOSPITAL, ENUGU.

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Keywords: Artemisinin combination therapy, malaria, UNTH, *Plasmodium falciparum*, Coartem®

ABSTRACT

This study describes the treatment of Malaria in Children at UNTH, Enugu using Artemisinin Combination Therapy (ACT) and considers the cost of the therapy as an important variable for its success.
Currently, combination antimalarial therapy has been advocated by the WHO to improve success in malaria treatment and limit the spread of resistance. The ACT is now the mainline therapy for malaria because of excellent parasite clearance, ability to combat multi-drug resistant malaria and significant reduction of transmission rate, hence a reduction on the burden of the disease in our community.
It is important that practicing medical doctors, medical students and even the general public be abreast of these new trends in antimalarial therapy seeing the enormous contribution of malaria to the high infant mortality of 25% and childhood mortality of 30% in the country. It accounts for high absenteeism among school children and a high disability adjusted life years (DALYs) lost!

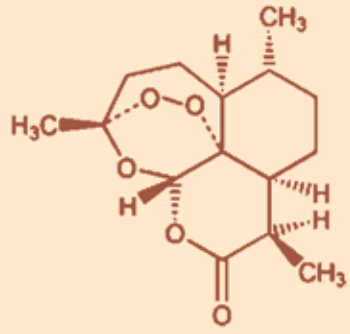
INTRODUCTION

Artemisinin *(Qinghaosu)*, the active antimalarial constituent of the Chinese medicinal herb, *Artemisia annua* was isolated in 1971. Its derivatives are fast acting and treat multi-drug resistant malaria. They are used in combination therapy to combat drug resistant *Plasmodium falciparum* malaria on the bases that drug resistance depends on mutation; the pfcrt K76T mutation primarily responsible for chloroquine resistance is virtually ubiquitous and the efficacy of chloroquine and SP (sulphadoxine/pyrimethamine) combination is similar to that of SP alone. If mutation is the issue, the probability of a parasite arising that is resistant simultaneously to two drugs with unrelated modes of action is the product of the per parasite mutation frequencies multiplied by the total number of parasites exposed to the drugs[1].

ARTEMISININ DERIVATIVES AND THEIR COMBINATIONS

Artemisinin undergoes a reduction reaction to dihydroartemisinin which gets converted to artemether (lipid soluble), artesunate (water soluble) and arteether (also called artemotil).
These derivatives act by inhibiting the *P. falciparum* encoded sarcoplasmic-endoplasmic reticulum calcium ATPase not by inhibiting the heme metabolic pathway as previously supposed[2]. They inhibit development of gametocytes and hence a potential reduction of the transmission especially of these resistant mutants.
Artemisinin based combination therapy for malaria is the simultaneous use of an artemisinin and another blood schizonticidal drug where both have different modes of action and different biochemical targets in the parasite. This has exploited the synergistic and additive potential of the individual drugs.
ACTs could be fixed combination therapy where components are co-formulated in the same tablet or capsule. For example:

1. Artemether/Lumefantrine (Coartem®, Riamet®)
2. Dihydroartemisinin/Piperaquine (Artekin®) currently available at about half the cost of Coartem® in Cambodia, China and Vietnam where it is used extensively[3].
3. Pyronaridine/Artesunate Currently said to be the most effective type of antimalarial therapy and should be in the market by 2008[4].
4. Chloproguanil-Dapsone/Artesunate



(i.e. LapDap/Artesunate).
ACTs can also be in free combination therapy where components are co administered in separately. Examples are;

1. Artesunate and Amodiaquine(Arsucam®, Larimal®, Dart®)
2. Artesunate and SP(Faranex®)
3. Artesunate and Mefluoquine.

TREATMENT OF MALARIA IN CHILDREN WITH ACT IN UNTH, ENUGU

ACTs are used as first line therapy in UNTH for the treatment of uncomplicated malaria. This is in consonance with the current national guideline on the treatment of malaria. Hitherto the treatment of uncomplicated malaria was with the use of monotherapies such as chloroquine, SP, artemisinin, Halofantrine. Due to increasing evidence of resistance to these antimalarial drugs a new policy was adopted in late 2005. The rationale for this combination therapy is to improve efficacy and to retard the development of resistance to the individual components of the combination. This concept of combination therapy has been realized in multiple drug therapy for leprosy, tuberculosis, cancer and more recently, in the antiretroviral treatments. The particular features of ACT relate to the unique mode of action of the artemisinin component, which includes the following:

- Rapid and substantial reduction of the parasite biomass
- Rapid parasite clearance
- Rapid resolution of clinical symptoms
- Effective action against multidrug resistant *P. falciparum*
- Reduction of gametocyte carriage, which potentially reduces transmission of resistant alleles.

ACTs are very expensive when compared with chloroquine and sp. With ACTs, the potential public health impact of reducing transmission is a factor to include in the evaluation of benefits versus costs. It is a well known fact that the affordability of drug is an important pharmacoeconomic index for the success of the therapy, so cost poses a challenge to the deployment of ACTs at community level.

In UNTH however, it is intriguing to know that Coartem®, a fixed combination regimen par excellence and WHO gold standard for ACT has been donated by the Christian Association of Nigeria (CAN) since April 2006. This is to

say that the drug is given free to affected children. It is available in sets for children weighing 5-15kg and 15-25kg. A child weighing less than 5kg is not treated with ACT for safety concerns.

It is important to understand that most of the treatment for malaria in our environment is provided outside the formal health sector, often by patent medicine vendors. Therefore subsidies by NGOs not reaching these places may still leave ACT unavailable to many patients, although presently there is a government policy that Coartem® should be given free in its health facilities. Also because of the cheap and available monotherapies for malaria, patients are treated for all febrile illness as malaria. This is probably because of high malaria endemicity in this area and so one of the first differential diagnoses for fever is malaria. It is thus safer to treat malaria even when it is not rather than leaving out some cases. If ACTs were to be used this way, the sustainability of any subsidy will be threatened. Cotecxin® was subsidized in UNTH by the government but it is now no more but this however may be due to the adoption of combination therapy as first line antimalarial regimen. For the sustainability of ACT, care should therefore be exercised in selecting febrile cases that are actually malaria knowing that the process of cultivation of the plant *Artemisia annua* from which the raw substance is extracted requires a minimum of six months; extraction, processing and manufacturing of the final product requires at least 2-

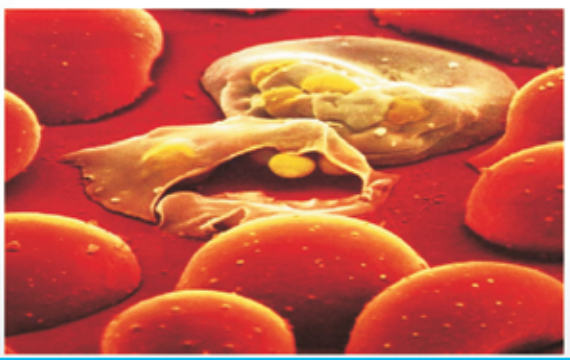
5months. While agricultural production is generally not regarded as a limiting factor, there is concern that the very rapid increase in demand for the pharmaceutical products, if not anticipated by agricultural production, can face shortage in supply of raw materials.
In the case of a child that presents with clinical evidence of severe malaria, treatment is with the use of intravenous quinine or other parenteral e.g. artemether and ACT is introduced as soon as the patient can tolerate oral medication. Even though this is the practice in UNTH, Enugu, it is important to emphasize at this juncture that in treating severe malaria, intravenous artesunate has been shown to be more rapidly acting than intravenous quinine in terms of parasite clearance; it is safe and simple to administer[5]. Treatment with artesunate h as also shown to be well tolerated, whereas quinine is associated with the induction of hyperinsulinaemic hyperglycaemia, a common serious complication. This is however prevented by double dilution of 50% dextrose solution given intravenously.
The main pharmacodynamic difference between artesunate and quinine is the much broader stage specificity of action of artemisinin compounds. Artesunate kills circulating ring parasites, which can be removed by the spleen whereas quinine does not[5]. artesunate furthermore, prevents maturation of the younger parasite stages and thereby prevents sequestration which reduces subsequent microcirculatory obstruction.
Generally speaking, results so far from ACT in children with malaria in UNTH, Enugu has been favourable. Failures resulting from improper usage, especially inadequate treatment duration cannot be blamed on drug efficacy. Therefore there is no scientific evidence of drug treatment failures in this centre.

WHAT ABOUT ARTEMISININ RESISTANCE?

When short courses (<5 days) of an artemisinin monothrerapy are used, the rate of recrudescence is high. This is not because of resistance in the parasite but because of drug properties; it is quickly eliminated from the circulation. In ACT, recrudescence is minimized by the partner drug, its efficacy and kinetics. Ideally ACT should be deployed before resistance to partner drug has emerged. If patient is infected with parasites resist ant to the partner drug, then the combination with artemisinin may only marginally improve the overall parasitological cure, because a 3 day course of artesunate is insufficient in itself. However the early response will be improved by the artesunate component. This is not to say that resistance to artemisinin will never happen, in fact resistant isolates have been produced in the laboratory[6].
Reports of treatment failure have emerged from artemether/lumefantrine in Zanzibar, with genetic evidence for the selection of lumefantrine resistant parasites[7]. The best way to protect the artemisinin derivatives from resistance is to combine them with another effective drug.
As regards efficacy, ACTs are the most efficacious regimen for preventing recrudescence but this benefit is outweighed by an increased risk of new infection. This is likely due to the fact that the artemisinin are rapidly eliminated leaving only their partner drug to provide the post treatment prophylaxis[7].

CONCLUSION

ACTs are needed to replace inadequate drug regimens that are leading to increased malaria related morbidity and mortality. They are also very important because artemisinin derivatives used in the combination reduces the transmission because of its gametocidal effect, thereby impacting significantly on the transmission rate of the parasite with a resultant reduction on the disease burden in our community.
Although the ACT worked very well on ongoing infections, for recurrent infections it does not perform better. In highly endemic areas like ours, recrudescence may be delayed, presumably due to contribution of host immunity on initial parasite clearance, and this delay appears to increase with increasing transmission intensity. For the control of recurrent infections, other control measures such as bed nets, vector reduction methods and possibly intermittent presumptive therapy (IPT) should be used as a way of reducing the risk of new infections and maximizing the impact of the therapy.
ACT is considerably more expensive than an older combination drugs (amodiaquine and SP). The current policy, if sustained will probably engender a cost effective method of control of malaria in the country at large. The problem will be the upscale of such provision (free antimalarial drugs) to non governmental health facilities.



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"SPECTRUM OF CHILDHOOD MALIGNANCIES IN ENUGU, NIGERIA (1999-2004)"

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ABSTRACT

A retrospective analysis of childhood malignancies in Enugu, Nigeria was carried out using data obtained from the Cancer Registry of the University of Nigeria Teaching Hospital (UNTH), Enugu between 1st January 1999 and 30th June 2004. A total of 79 childhood cancers were recorded during the period. There were 48 males (60.8%) and 31 females (39.2%) with a male female ratio of 1.5:1. The three commonest malignancies were lymphomas 33 (41.2%), sarcomas 12 (15.2%) and nephroblastomas 12 (15.2%). The less common tumours included the leukaemias 6(7.6%), retinoblastomas 6 (7.6%), neuroblastomas 4 (5.1%), and carcinomas 2 (2.5%). Burkitt's lymphoma remains the commonest specific childhood malignancy in this environment constituting 19 (57.6%) of all the lymphomas and 24.1% of all the cancers seen.

Key words: childhood, malignancy, Enugu, Nigeria.

Introduction

With sustained improvement in the control of communicable infections and malnutrition in Africa, it is becoming evident that neoplastic disorders account for a significant proportion of childhood morbidity and mortality[1,2,3]. According to the latest World Cancer Report[4], more than half of the global cancer burden is experienced in developing countries, although incidence rates in such countries are low compared to those in developed countries. It is therefore very important to sustain the focus on research on the role of non-communicable diseases such as cancer on childhood morbidity and mortality. This is necessary for rational planning and appropriate investment in prevention and early detection[4]. We hereby present the current pattern of childhood malignancies seen at the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria. We have also compared the findings with previous studies from the same centre.

Materials and methods

A retrospective analysis of childhood malignancies in Enugu, Nigeria was carried out on children who were 15 years and below. Data was obtained from the Cancer Registry of the University of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria between 1st January 1999 and 30th June, 2004. Only patients recorded in the Cancer Registry were included in this study. The information available were diagnosis, sex, age and site of tumour.

Results

A total of 79 children with ages 15 years and below with various malignancies were found. There were 48 (60.8%) males and 31 (39.2%) females giving a male female ratio of 1.5:1. Thirty three of the patients (41.8%) were below 5 years of age. Table 1 shows the relative frequencies of childhood cancers seen during this study period.

The youngest patient, who had sacrococcygeal teratoma, was 3 months old. Ten (83.3%) of the patients with Wilms' tumour were below 5 years of age with 9(75%) of them being 3 years and below. Tables 2 and 3 show the age and sex distribution of the patients respectively.

The three commonest malignancies were lymphomas 33(41.2%), sarcomas 12(15.2%), and nephroblastomas 12(15.2%). The less common tumours were the leukaemias 6(7.6%), retinoblastomas (7.6%) and neuroblastomas 4(5.1%). The most common malignancies were the malignant lymphomas which constituted 41.2% of all the tumours seen. Among the 33 malignant lymphomas, there were two cases of Hodgkin's lymphoma constituting 6.1% of the lymphomas and 2.5% of all the cancers. These were in two boys aged 12 and 7 years. Non-Hodgkin's lymphoma(NHL) therefore constituted 31(93.9%) of the lymphomas. Of the non-Hodgkin's lymphomas, Burkitt's lymphoma(BL) was the commonest. There were 19 cases of BL which constituted 24.1% of all the tumours and 57.6% of the malignant lymphomas. Overall, Burkitt's lymphoma was therefore the single most common specific cause of childhood malignancy during this five and a half year review. The 19 cases of Burkitt's lymphomas were made up of 13 males and 6 females giving a male-female ratio of 2.2:1. The sites of distribution of 17 BL cases are as shown in Table 4. The site of affectation in 2 of

the BL cases were not stated in the Cancer Registry data. Their clinical records files could not be traced to ascertain the sites involved. Ten (58.8%) of the 17 BL patients,8 boys and 2 girls, had abdominal presentation, either alone or in combination facial and central nervous system(CNS) involvement. Fourteen(82.4%) of the patients,9 boys and 5 girls, had facial involvement, either alone or in combination with abdominal and CNS involvement. Facial presentation was the single commonest mode of presentation constituting 41.2% of the BL patients. Five (26.3%) of the Burkitt's lymphoma patients were below 5 years, made up of 3 males and 2 females.

The sarcomas formed the second commonest paediatric malignancy constituting 12 (15.2%) of the tumours seen. The highest prevalence was in the 0-5 years age group. There were 7 males and 5 females with a M:F ratio of 1.4:1. The commonest sarcomas were the rhabdomyosarcomas which made up 6 (50%) of the sarcomas and 7.6% of all the neoplasms. There was only one case of Kaposi's sarcoma constituting 8.3% of the sarcomas and 1.3% of all the neoplasms seen.

Nephroblastoma was the third commonest cause of paediatric cancers constituting 15.2% of all the tumours seen. There were 6 females and 6 males with a M:F ratio of 1:1. Ten (83.3%) of the nephroblastomas occurred in children below 5 years of age. The oldest of the patients with Wilms' tumour was 11 years old. Retinoblastomas and leukaemias each constituted 6(7.6%) of all the cancers seen during the period of this study. All the cases of retinoblastoma occurred below 10 years of age with a M:F ratio of 1:1.

The 6 leukaemic patients were made up of 5 cases of acute lymphoblastic leukaemia and a case of chronic myeloid leukaemia. There was only one male leukaemic patient and 5 female patients.

Four patients (5.1%) had neuroblastoma and they were 2 males and 2 females who were all below 10 years of age. There were 2 carcinomas-a renal cell carcinoma in a 4 year old boy and an ovarian carcinoma in a 4 year old girl.

Discussion

In this review of childhood cancers at UNTH, Enugu, Nigeria, 79 cases of paediatric tumours were recorded in the Cancer Registry over a period of 5 ½ years giving an average of 14.4 cases per year. This is lower than the figure of 31.3 cases per year reported by Onwasigwe et al from the same centre in 2002[5] in a study covering the period between 1989 and 1998. Other previous reports from this centre also showed higher figures of 116.4(1976-1980)[6] and 51.4(1978-1982)[7] cases per year respectively. It does appear from these various reports that there is generally, a declining frequency of childhood cancers in this environment. A possible explanation however is the establishment of newer Teaching Hospitals in the Eastern region of Nigeria which may have been taking up some of these patients that would otherwise have presented to this centre. Whether this overall decline in the frequency of childhood cancers in this centre is real or not will require further study. Although this annual cancer frequency of 14.4 is much less than the 104.5 cases per year (1881 cases over 18 years) reported from Ibadan[8], western Nigeria, it compares well with the 12 cases per year reported from Calabar[9] another centre in south-eastern Nigeria in 1992. The general pattern of distribution of childhood cancers in this study is similar to what has been obtained in other Nigerian and African studies[2,3,6,9,10] with a low relative frequency of leukaemias and intracranial tumours compared with the caucasian populations. The review from Ibadan, Nigeria[8] however noted an upsurge in the relative frequencies of intracranial neoplasms but none was seen in this centre during this study period. This could be due to the fact that University College Hospital, Ibadan, Nigeria, being the centre of excellence in the neurosciences is a referral centre for the neurosurgical disorders. The upsurge in the relative frequencies of intracranial neoplasms in Ibadan compared to results from other Nigerian and African studies most probably reflects the high concentration of neurosurgeons as well as adult and paediatric neurologists in that centre[8].

Lymphomas

Lymphomas remain the commonest childhood malignancies in this environment, constituting 41.8% of all the cancers seen. Burkitt's lymphoma also remains the single specific most common childhood tumour constituting 19(57.6%) of all the lymphomas and 24.1% of all the malignancies. This is consistent with previous reports from this centre where lymphomas formed 38.3%[5] and 40%[7] and Burkitt's lymphomas made up 25.3%[5] and 26.8%[7] of all the cancers seen. There were 13 male and 6 female patients with Burkitt's lymphoma giving a male female ratio of 2.2:1. This is similar to the 2:1 ratio obtained in a Malawian study[2] but contrasts with the ratio of 1.6:1 obtained in a previous study from this centre[5] and 1.4:4 obtained from another centre in Tanzania[3]. However, there is no doubt from these studies that there is a male preponderance. Just as it was noted in a previous study from this centre[6], Burkitt's lymphoma was rare in the first two years of life in this study. Only one patient was aged 2 years in this study and she was the youngest of the Burkitt's lymphoma patients. This study also shows further decline in the relative frequency of Burkitt's lymphoma even though it remains the commonest childhood malignancy. In this series, the relative frequency of Burkitt's lymphoma is 24.1% of all the malignancies compared with 25.2% of the study carried out between 1989 and 1998[5] and the 37.0% obtained in an earlier study carried out between 1976 and 1980[6].Contrary to a previous report from this centre by Oguonu et al[11] where

abdominal tumours were the predominant mode of presentation, this study shows a facial predominance. However, our findings support another report from this centre by Oji et al[12] which showed a facial predominance. Other reports from Jos[13], Sokoto[14] and Ibadan[15] showed predominance of abdominal presentation. The facial presentation is usually more striking, tending to make the patients present early[12]. This is because facial tumours disfigure the face. The diagnosis of facial tumours is also easier to make than abdominal tumours because of easier accessibility for aspiration and biopsy for cytological and histological diagnoses.

Sarcomas

In a previous report[5] from this centre, sarcomas were also the second commonest malignancy but the frequency obtained in that report was 14.7%. In another earlier report[6], sarcomas were the third commonest cause of childhood malignancy constituting 10.4% of the tumours seen. This therefore suggests that there has been a consistent rise of sarcomas in children in this environment. In all the three studies, rhabdomyosarcomas were the commonest of all the sarcomas seen. The sarcomas occurred in all the age groups but the highest frequency was in the age group between 0 and 5 years unlike in the earlier report[6] where the highest frequency was seen in the ages between 6 and 11 years. This also contradicts the Ibadan study[8] where the highest frequency occurred in the age range between 10 and 14 years.

Nephroblastomas

The relative frequency of nephroblastoma of 15.2% in this study is comparable with the 14.1% obtained in a previous study[5] but less than the 19.6% of an earlier report[6], all from this centre. It is also similar to the figure of 16.7% obtained from studies in Calabar[9], Nigeria and Malawi[16].

Leukaemias

Leukaemias constituted 7.6% of all the cancers seen in children during the period under study. Reports from this centre in 1986[6] and 2002[5] showed relative frequencies of leukaemias of 5.4% and 8.6% respectively. These figures are still lower than figures from developed countries where leukaemias constitute about one-third of childhood malignancies[17,18].In developed countries, most of the childhood leukaemias occur below 5 years of age predominantly in boys[19], contrary to what has been obtained in this study where most of the patients are girls and are above 5 years. We may however expect to see more cases of leukaemias as more haematologists and diagnostic facilities become available in this centre.

Retinoblastomas

The relative frequency of retinoblastomas of 7.6% in this study is less than the 12.1% obtained in the previous study from this centre by Onwasigwe et al[5] but certainly more than the earlier figure of 2.9% reported by Agugua et al[6]. The pattern of occurrence of retinoblastomas in this environment is not yet clear and further studies in this area are encouraged.

Neuroblastomas

The relative frequency of 5.1% obtained for neuroblastomas in this study is comparable to the figure of 5.6% earlier obtained by Agugua et al[6] but higher than that of 1.9% obtained by Onwasigwe et al[5]. In one of the studies from Ibadan, Nigeria[1], the relative frequency of neuroblastomas was 2.6%. Overall, the relative frequency of neuroblastomas is still low in this environment compared to American blacks[20] where neuroblastomas alone accounted for 9.3%.

In summary, this present study has revealed that lymphomas remain the commonest childhood malignancy in this environment with Burkitt's lymphoma constituting the commonest specific paediatric tumour. A relative decline in the frequency of Burkitt's lymphoma is however noted. There is a rising relative frequency in the occurrence of sarcomas, nephroblastomas and leukaemias. There is however a decline in the relative frequency of retinoblastoma. The present study also confirms that the relative frequency of neuroblastoma is lower in this environment than Caucasian figures[1,20]. Further studies will need to be carried out in the general population to ascertain the true picture of the distribution of childhood tumours in this locality since this is a Hospital based study.

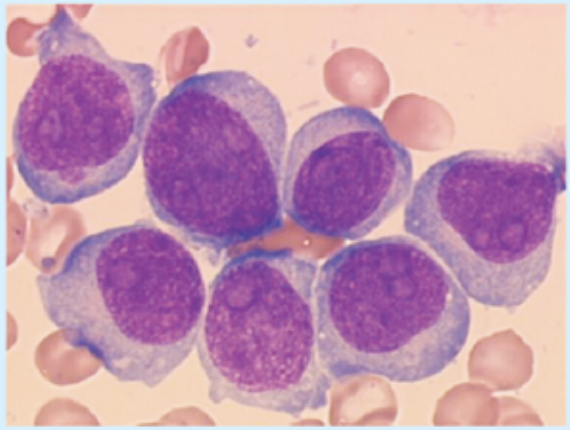

Table 1: Relative frequencies of childhood cancers seen in UNTH Enugu, 1999- 2004.

Malignancy	Number	Percentage
Lymphomas	33	41.2
(Burkitts lymphoma)	(19)	(24.1)
Sarcomas	12	15.2
Nephroblastomas	12	15.2
Leukaemias	6	7.6
Retinoblastomas	6	7.6
Neuroblastomas	4	5.1
Carcinomas	2	2.5
Teratoma	1	1.3
Unclassified	3	3.8
Total	79	100

Table 2: Age distribution of childhood cancers in UNTH Enugu 1999-2004.

Malignancy	0-5yrs	5-10yrs	10-15yrs	Unstated	Total
Lymphomas (Burkitts lymphoma)	7 (5)	12 (7)	14 (7)		33 (19)
Sarcomas	5	3	4		12
Nephroblastomas	10	1	1		12
Leukaemias	1	3	2		6
Retinoblastomas	4	2			6
Neuroblastomas	3	1			4
Carcinomas	2				2
Teratoma	1				1
Unclassified			2	1	3
Total	33	22	23	1	79

Table 3: Sex distribution of childhood cancers in UNTH Enugu 1999-2004

Malignancy	Male	Female	M:F ratio
Lymphomas (Burkitts lymphoma)	25 (13)	8 (6)	3.1:1 (2.2:1)
Sarcomas	7	5	1.4:1
Nephroblastomas	6	6	1:1
Leukaemias	1	5	0.2:1
Retinoblastomas	4	2	2:1
Neuroblastomas	2	2	1:1
Carcinomas	1	1	1:1
Others	2	2	1:1
TOTAL	48	31	1.5:1

Table 4: Site of tumour distribution among 17 Burkitt's lymphoma patients

	Number of cases.		
Site	Male	Female	Total No.(%)
Face only	3	4	7 (41.2)
Abdomen only	2	1	3 (17.6)
Abdomen and face	2	-	2 (11.8)
Abdomen, face, CNS	4	1	5 (29.4)
Total	11	6	17 (100)

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THE THREAT OF HEPATITIS C

A Review of its Implication for the Developing Africa

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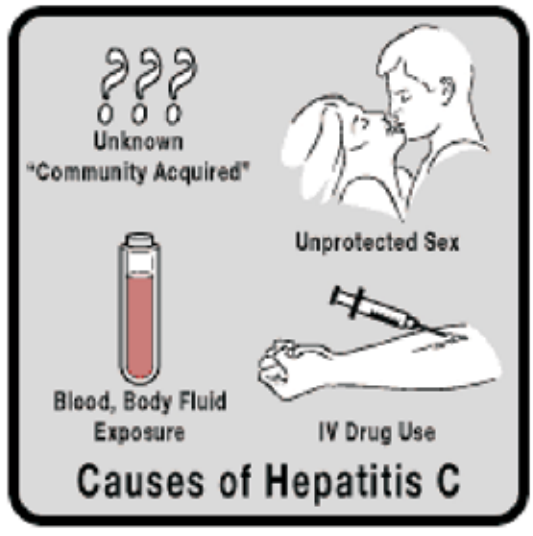
Keywords: Hepatitis C, HCV, Africa, Epidemiology

Abstract

Hepatitis C virus [HCV] is a major etiologic agent of chronic hepatitis and it is a major cause of morbidity and mortality. At least 85% of patients infected by HCV go on to develop chronic liver disease. Cirrhosis develops in about 15-30% of these within 10 to 30 years and of these patients between 7% and 15% will develop hepatocellular carcinoma.

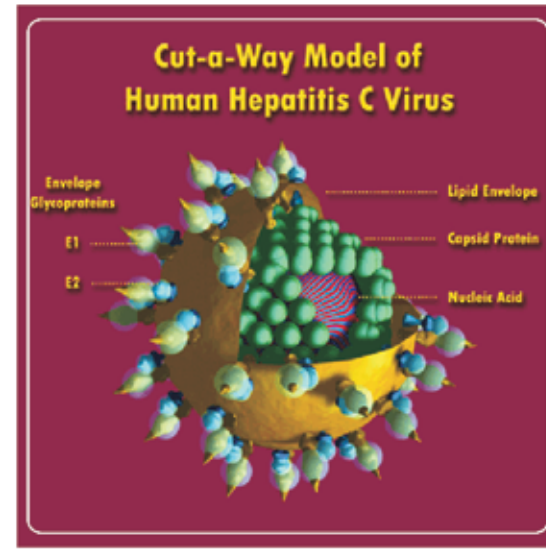
The prevalence of HCV infection in Africa is not well established probably due to poor screening, diagnosis and under reporting of diagnosed cases. Owing to this, the burden of HCV infection in Africa can only be inferred from epidemiological data in regions where it is established and correlated with epidemiological factors inherent in Africa. However, recent reports suggest that the prevalence of HCV infection in normal Africans may be as high as 10.9%.

Prevalence and population-based studies have suggested that complications of the liver disease associated with chronic hepatitis C infection may potentially require substantial health care resources and generate very high costs for medical systems worldwide and this poses a big threat to economies in transition. Careful understanding and assessment of hepatitis C health and its economic burdens are likely to guide better programs for the screening and diagnosis of HCV infection, management of infected individuals and the prevention of complications.



Introduction

HCV was identified in 1988 and was found to be responsible for 70-90% of post transfusion hepatitis[1].It was before then called the non-A, non-B hepatitis. HCV is a hepacivirus and occupies a genus in the flaviviridae family. HCV is an enveloped single stranded RNA virus with a genome that codes for a single polyprotein that is subsequently processed into functional structural proteins (a highly conserved nucleocapsid core protein and two envelop proteins, E1 and E2) and non-structural proteins. RNA polymerases, the enzymes that synthesize RNA in contrast to DNA polymerases have poor fidelity and because of this, the virus is inherently unstable.



One of the major problems with HCV infection is that 85% of individuals initially infected with this virus will become chronically infected, usually for decades. The other 15% of hepatitis C virus infected individuals simply have an acute infection; that is, one that resolves spontaneously in a few weeks or months. The propensity of hepatitis C virus to cause chronic infection is explained by the extraordinary ability of this virus (in contrast to most other viruses, including hepatitis A) to avoid destruction by the body's immune defense system[2].

Once established, chronic HCV infection causes an inflammation of the liver called chronic hepatitis. This condition can progress to scarring of the liver, called fibrosis, or more advanced scarring, called cirrhosis. Some patients with cirrhosis will go on to develop liver failure or the complications of cirrhosis, including liver cancer. Male patients, patients over 40 years and those with genotype1 and 4 of HCV have more rapid development of fibrosis[1].

Epidemiology

"We stand at the precipice of a grave threat to our public health... It affects people from all walks of life, in every state, in every country. And unless we do something about it soon, it will kill more people than AIDS."

- C. Everett Koop
Former U S Surgeon General

It is estimated that close to 200 million individuals in the world are infected with HCV. The prevalence of HCV infection varies in different parts of the world. It is less than 0.5% in the Scandinavia whereas it is up to 20% in Egypt[2]. Since HCV virus infects people from all walks of life the distribution of the infection will correspond to practices that predispose to its transmission. It is known that about 3.9 million Americans or 1.8% of the population has antibodies against HCV. Fully 70% of these or 2.7 million have evidence of chronic infection as determined by the presence of viral RNA in the serum. This makes HCV the most common chronic blood-borne infection and accounts for almost half of all patients in the U.S with chronic liver disease[3]. The data in Africa is not well established but recent reports suggest a prevalence of about 10.9% in normal Africans[4]. Hepatitis C is transmitted most efficiently through the blood. In the U.S intravenous drug use accounts for up to 60% of cases, blood transfusion 10%, other modes of transmission are hemodialysis, accidents with contaminated sharp objects in health care workers, transplantation of infected solid organs and other practices that predispose to direct inoculation of infected blood. Sexual transmission, perinatal transmission and horizontal transmission in childhood are not common when compared to that of HBV.

Egypt has the highest prevalence of HCV infection in the world and this is not unrelated to parental antimony treatment of schistosomiasis that was endemic in Egypt. The Egyptian Ministry of Health estimated the national prevalence rate of HCV antibody positivity in 1999 to be 18.9%. In addition to blood transfusions prior to 1994, the major risk factor associated with the HCV infection is the history of antischistosomal injection treatment[5]. From the foregoing, it can be deduced that the major risk group in Africa are recipients of blood transfusion and patients on chronic transfusion such as sickle cell disease and â-thalassemia patients.

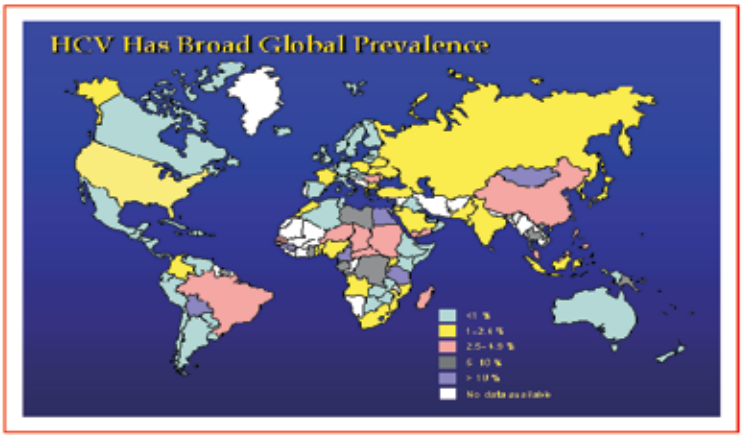


Table 1 **Hepatitis C, prevalence rates based on published reports, by country/area**

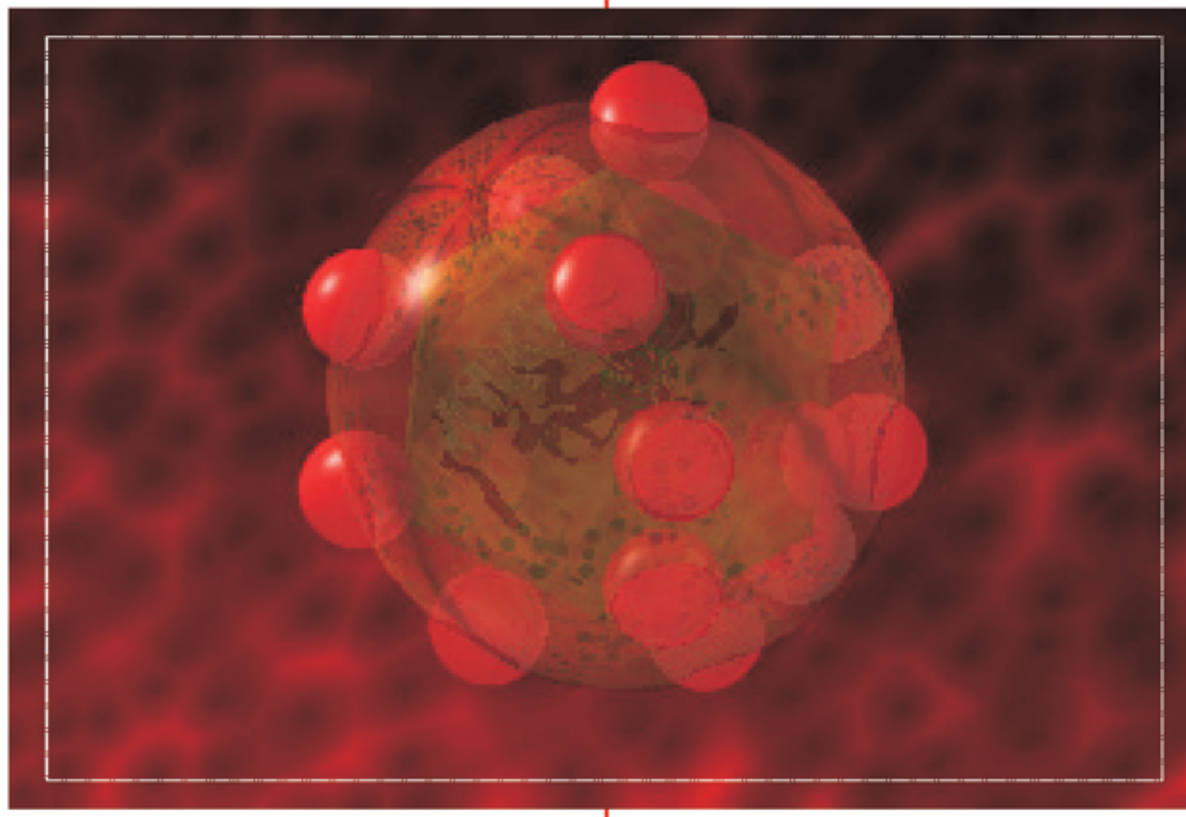
Country/area	Rates (%)
Algeria	0.2
Angola	1.0
Benin	1.5
Botswana	0.0
Burundi	11.1
Cameroon	12.5
Central African Republic	4.5
Chad	4.8
Democratic Republic of the Congo	6.4
Egypt	18.1
Ethiopia	0.8
Gabon	6.5
Ghana	2.8
Guinea	10.7
Kenya	0.9
Madagascar	3.3
Mauritania	1.1
Mauritius	2.1
Morocco	1.1
Mozambique	2.1
Niger	2.5
Nigeria	1.4
Papua New Guinea	0.6
Rwanda	17.0
Senegal	2.9
Sierra Leone	2.0
Somalia	0.9
South Africa	1.7
Sudan	3.2
Swaziland	1.5
Togo	3.3
Tunisia	0.7
Uganda	1.2
United Republic of Tanzania	0.7
Zambia	0.0
Zimbabwe	7.7

Table 2 **Hepatitis C, estimated prevalence rate and number infected, by WHO region**

WHO region	Total population (millions)	Rate (%)	Infected population (millions)	No data available (number of countries)
Africa	602	5.3	31.9	12
Americas	785	1.7	13.1	7
Eastern Mediterranean	466	4.6	21.3	5
Europe	858	1.03	8.9	19
South-East Asia	1 500	2.15	32.3	3
Western Pacific	1 600	3.9	62.2	11
Total	**5 811**	**18.7**	**169.7**	**57**

Tables 1 & 2 show updated hepatitis C prevalence data submitted to WHO by some countries/areas in Africa as of June 1999. Because of differences in the population groups studied, methods of data collection and interpretation between countries, and since only limited data are available for some countries, the prevalence shown does not necessarily represent the true prevalence in a country[6].

Although the introduction of routine screening of blood, blood products and organ tissues has substantially reduced transmission, unscreened blood and blood products are still being used in many developing countries or economies in transition. The prevalence of hepatitis C in some countries in Africa remains high compared to industrialized countries



Contaminated sharp object injuries are a major source of HCV infection among health care workers, accounting for almost 40% of HCV infections in that group, having caused 16,000 infections worldwide in the year 2000. It has also been reported that most deaths in health care workers resulting from accidents with contaminated sharp objects (not HCV alone) occur in sub-Saharan Africa [7].

To estimate mortality from HCV infections, 63% of persons infected before the age 40 years were assumed to progress to chronic infection, with a cumulated incidence rate of cirrhosis of 5% at 20 years and a yearly mortality rate associated with chronic liver disease of 3.7% after the onset of cirrhosis. In persons infected after the age of 40 years, the assumed rate of progression to chronic infection was 80%, the cumulated incidence rate of cirrhosis of 20% at 20 years and the yearly mortality rate remained the same as in the younger age group[7].

Molecular Epidemiology

Due to the inherent instability of the HCV RNA, HCV is characterized by a high degree of nucleotide sequence variability. HCV has a 9-kb genome that codes for a single polyprotein. The protein is subsequently processed into functional proteins. Overall, the heterogeneity of the viral genome ranges from 30 to 35% between different genotypes and has been used to define three types of regions: highly conserved regions (e.g., the 5' untranslated region), variable regions (e.g., envelope 1 [E1] and nonstructural 5b [NS5b]), and hypervariable regions (HVR) (e.g., HVR1 and HVR2 in E2)[8].

HCV is generally classified into 6 major genotypes and around 100 subtypes. Certain genotypes are more prevalent in some geographical areas: Genotype 4 in north and central Africa, genotype 1 in West Africa and genotype 5 in south Africa[9].

The classification into six major genotypes has been accepted, and there is further intrasubtype and intrasubject heterogeneity[10].

The development of an effective HCV vaccine to protect humans from HCV infection and chronic liver disease is a public health priority, yet differences in antigenic epitopes in genotypes, subtypes, and quasispecies could make cross-protection unlikely.

It has also been observed that certain variants respond poorly to available prophylactic treatment modalities and genotype 1, which is prevalent in West African countries, has been implicated[2]. Patients with genotype1 and 4 of HCV have more rapid development of fibrosis[1]. Interestingly genotype 4 represents over 90% of the cases in Egypt[6].

Discussion

Hepatitis C is one of the infectious diseases described in the '80s for which there is no cure and no preventive vaccination. Sub-Saharan Africa accounts for nearly half of infectious disease deaths globally and will remain the most vulnerable region. The death rates for many diseases, including HIV/AIDS and malaria,

exceed those in all other regions. Sub-Saharan Africa's health care capacity is the poorest in the world and will continue to lag. Given these statuses, the threat of HCV is grave because development of an effective surveillance and response system is at least a decade or more away owing to inadequate coordination, funding and lack of workforce at various national levels. Although overall global health has improved substantially in the recent decades, the gap between the rich and the poor in terms of availability of quality health care system is very wide. While the incidence of HCV infection should decrease in the developed world, it is only expected to increase in the underdeveloped and most of the developing countries. Reasons for this being that cases are under reported, screening policy is very poor and the management of HCV infection is quite costly and also requires a health care system which is very responsive; these can only be achieved in very few African countries.

Given the course of the disease of hepatitis C, most infected people presently may remain asymptomatic for up to ten years. The hepatitis C burden will continue to grow for at least another decade due to the disease's long incubation period, with the number of deaths possibly surpassing HIV/AIDS deaths even though the rate of new infections should drop in countries where blood is screened for the antibodies to HCV. A worse scenario is expected in some other African countries where the screening policy has not been adopted and enforced.

Lack of awareness of the HCV infection in most African countries is a factor that has a major impact on the HCV burden. Some cultural and traditional practices still increase the risk of transmission using contaminated penetrating instruments. Gaps in knowledge relating to the epidemiology, transmission routes and disease burden of hepatitis C in Africa warrant surveillance of the disease, in order to determine specific health care measures for prevention and control.

The infected populations are mostly unaware of their status and thus are more likely to come down with the complications. This is because patients do not develop symptoms until they have progressed to advanced cirrhosis. In view of this, early diagnosis of the disease is essential to curb the progression of the disease. Aid programs to prevent and treat the HCV disease in African countries depend largely on national policy makers and indigenous health workers for their success and cannot be fielded effectively in their absence. Educational programs aimed at preventing disease exposure frequently depend on higher literacy levels and require cultural and social factors that are often absent.

Finally, The impact of HCV infection over the next 20 years will be heavily influenced by three sets of variables. The first is the implementation of policies for screening of blood and blood products for HCV and its success. The second is the course of developing economies, especially concerning the basic quality of life of the poorest groups in these countries. The third is the degree of success of global and national efforts to create effective systems of surveillance and response. The interplay of these variables will determine the overall outlook.

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ALLERGIC CONJUNCTIVITIS

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Keywords: Allergic conjunctivitis, vernal keratoconjunctivitis, Atopic keratoconjunctivitis, Giant papillary conjunctivitis, Contact dermatoconjunctivitis.

Abstract

Ocular surface inflammation due to allergy is one of the commonest eye disorders. It shows a male preponderance and tends to start in the first and second decade of life .The cardinal symptom is itching which is usually bilateral. In about 50% of cases, there is presence of positive family history. This article reviews the common types of allergic conjunctivitis, pathogenesis, clinical features, and treatment

Introduction

Allergic inflammation of ocular surfaces (lid margins, conjunctiva and cornea) is one of the commonest eye disorders. This allergic disorder consists of a spectrum of disease, which could be acute or chronic, seasonal or perennial, mild or severe. Though most of these conditions do not affect vision and resolve with time, some are associated with vision impairment and could cause vision loss.

Classification of allergic conjunctivitis

1. Seasonal Allergic conjunctivitis (Hay fever)
2. Perennial Allergic conjunctivitis
3. Vernal keratoconjuctivitis (spring catarrh)
4. Atopic keratoconjunctivitis
5. Giant papillary conjunctivitis
6. Contact dermatoconjunctivitis

Seasonal Allergic Conjunctivitis and Perennial Allergic Conjunctivitis

Seasonal allergic conjunctivitis seasonal and perennial allergic conjunctivitis are the two types of acute allergic conjunctivitis (AAC). AAC is a recurrent condition whereby seasonal airborne allergens such as pollens from ragweed, grasses, trees and weeds or persistent allergens like animal dander, house mites cause mast cells (MC) degranulation and features of the disease .Also MC releases enzymes such as histaminases with helps to shut off the degranulation of MC and thus limiting it. .Only on severe conditions do these mechanism become complex, causing releasing of secondary mediators that further stimulates degranulation, cell infilteration and inflammation. It could be seasonal (SAC) or perennial (PAC) when it last throughout the year.

Clinical Features

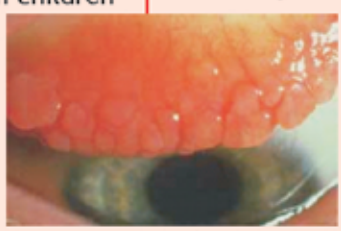
AAC is usually characterized by intense itching, tearing, watery discharge, burning sensation (seasonal variations depending on the type).
Signs include chemosis (conjuctival edema), swelling of eyelids, and dilatation of conjuctival vessels. Clinical signs may be absent though.
There may be also sign of rhinitis symptoms. There is no conjunctiva papillary reaction and rarely conjunctival opacification

Vernal keratoconjunctivitis (VKC) and Atopic keratoconjunctivitis(AKC).

Vernal, derived from the Greek meaning "occurring in the spring," is a chronic bilateral inflammation of the conjunctiva. It is most commonly found in children and adolescents. Males tend to be more affected than the females. It usually resolves by early adulthood though severe cases can persist and lead to blindness. VKC is more prevalent in areas that are hot and dry such as the Middle East, the Indian subcontinent and Africa. It is virtually absent in the cold climate. A survey of VKC conducted in the University of Benin Teaching Hospital from January 1, 1997 to December 31, 1998 showed that VKC is the most common conjunctivitis. Age range of patients was 5 months to 38years with the peak incidence at 15.5 ± 8.3years. It is common between April and August though severe cases can be perennial.
The immunopathogenesis mechanism is complex and involves an IgE and Th2 cytokine profile
AKC is a chronic external ocular inflammation but occurs late in teenage years and continues for 4-5 decades. The peak incidence is at 30-50 years. AKC, though rare, is an important differential diagnosis of VKC and the most disturbing of all allergic conjunctivitis. The symptoms last almost throughout the year. AKC pathogenesis is not fully understood but some investigators proposed complex immunomodulated dysfunction

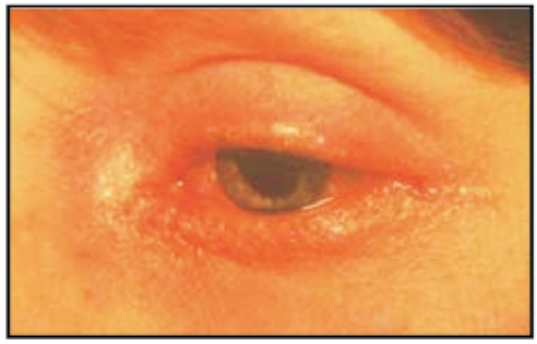
Clinical features

Symptoms of VKC include itching, extreme irritation, pain and photophobia (because of involvement of cornea), foreign body sensation and ropy mucous discharge.
The signs include the presence giant papillae on the superior tarsal conjunctiva, this simulates cobble stone appearance.



Upper tarsal surface in vernal keratoconjunctivitis showing 'cobblestone' appearance.

Symptoms of AKC are same as VKC but there is usually the presence of atopic dermatitis, exudative vesicular or crusted lesions on the body. Eczema, rhinitis, asthma and chronic blepharitis may be present. The papillae are seen mainly on the inferior palpebral conjunctiva though some may appear on the superior palpebral conjunctiva



The eyelids in atopic keratoconjunctivitis

Giant Papillary Conjunctivitis.
This is becoming increasingly popular with the advent of extended wear lenses. It is also associated with sutures in the eye following intracapsular cataract extraction, intracapsular lens implantation and ocular prosthesis. It tends to affect young patients more.
Clinical features
Symptoms include reduced tolerance of wearing the contact lens, foreign body sensation, excess mucous discharge, blurred vision due to accumulation of mucus on the nasal part of the eye.
Signs include presence of giant papilla of upper palpebral conjunctiva, chemosis, blepharoptosis; the conjunctiva is initially translucent but later opaque. It is commoner in patients using hard lens. GPC is due to allergic reaction to the proteins that coats the lens. Contact lens wearers secrete these proteins.

Contact Dermatoconjunctivitis.
This is contact allergy of the eye and periocular area that occurs with a variety of cosmetics, soaps, contact lens solutions and medications.
Clinical features
Symptoms include itching, periorbital swelling, and redness of conjunctiva. Substances commonly causing dermatoconjunctivitis include neomycin, atropine, papain, bacitracin, polymixin B, and thiomersal in contact lens solutions, benzalkonium chlorides, and idoxuridine.

Diagnosis of Allergic conjunctivitis (AC)
Diagnosis of AC is highly dependent on a high index of suspicion and a good history. Symptoms of bilateral itching of the eyes associated with atopic respiratory tract disease are strong indications for allergy.
A History
1. The age, time of onset of symptoms, duration, recurrence of episodes and exacerbating factors.
   VKC is commoner in children while AKC is usually seen in adults. SAC and VKC usually have seasonal variations though severe cases of VKC may be perennial. In PAC due to dust mite allergy, symptoms usually worsen in the night and morning due to long exposure to mattress.

2 Bilateral itching, tearing, burning sensation, photophobia and blurred vision.
   Unilateral symptoms are strong evidence against allergy. Presence of photophobia and blurred vision suggest VKC and AKC

3 Nature of discharge.
   Clear white stringy discharge strongly suggests an allergic disorder while mucopurulent discharge suggests infectious conjunctivitis.
   Sexual history should be inquired because the presence of associated urogenital symptoms may suggest Chlamydial infection or Gonococcal infection.
4 Family history of atopy, such as rhinitis, asthma or eczema may be present
5 Use of any topical eye medication and solutions, recent change in cosmetics: skin creams
6 History of wearing contact lens, recent eye surgery and use of preservative for Cleaning the lenses.

B Investigations
1. Skin prick test used to confirm the culprit allergen especially if the patients works with animals

2. A patch test in suspected cases of contact dermatoconjunctivitis
3. Conjunctival scraping looking for eosinophils in suspected cases of PAC and SAC.

Management
This consists of non-pharmacotherapy and pharmacotherapy.
A. Non-pharmacotherapy
1. Causative agent should be identified and there should be environmental control; avoiding allergens

2. Use of cold compresses; splashing of cold water on the eye may be all that is necessary in mild SAC and PAC.

3. Not rubbing the eyes

4. In GPC, removal of the contact lens or foreign body usually results in resolution. Lens cleaning agents should be preservative free.

B. Pharmacotherapy
1. SAC and PAC
   Anti histamines and vasoconstrictors help to reduce the symptoms and signs. Mast cell stabilizers may be added when the anti

histamine fails.
Short-term steroid therapy for severe cases.

2. VKC and AKC.
   Mast cell stabilizers act as steroid sparing agents. Cromolyn Sodium is the longest established of these drugs. Both 2% and 4% drops are available for use up to four times per day.
   Short-term steroids are used in AKC and VKC for flare-ups.
   Cyclosporine has been found useful in severe blinding VKC and steroid resistant VKC and in AKC.

Surgery is usually limited to the treatment of sight reducing corneal disease in AKC and VKC Laser surgery is useful in corneal plaques.

Complications
Acute allergic conjunctivitis (SAC and PAC) usually resolve without any impairment in vision but severe cases of VKC and AKC could cause usual impairment or even loss of vision.
Corneal scarring, suppurative keratitis and cataract have been recorded in these patients. Blindness due to VKC and AKC are caused by corneal epithelial and stromal defects and scarring. This blindness could also be due to complications of topical steroids that increase the risk of corneal lesions becoming infected, vascularized, increased intraocular pressure and glaucoma in some patients karactogenesis and keratoconus may result.

Conclusion
Allergic conjunctivitis is one of the commonest eye disorders. In most cases, resolution is spontaneous with time while few can persist and cause visual impairment especially severe cases of AKC and VKC. The suggested treatment is not rigid but depends on the physician and patient with the cost being an important factor. More so the risk of complications associated with steroid therapy should be considered whenever it is prescribed.
Finally, the role of good history cannot be over emphasized.

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TRASTUZUMAB IN TREATMENT OF BREAST CANCER

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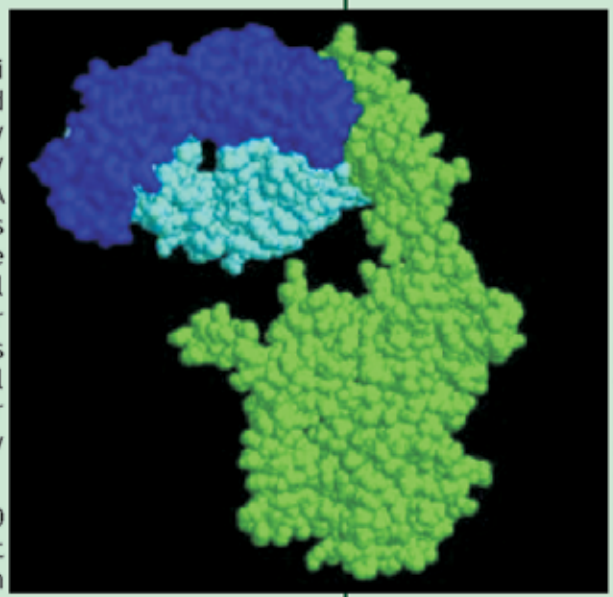
INTRODUCTION



Trastuzumab(Herceptin®) is a humanized monoclonal antibody produced by recombinant DNA technology that binds specifically to the human epidermal growth factor receptor 2 protein(HER 2) that is found on the cell surface of some cancer tumours, most notably breast cancer.[1]

About 20 to 30 percent of breast cancers produce an overabundance of HER 2 which is a growth promoting protein. The abundance of HER 2 on the surface of tumour cells causes them to divide very frequently. These tumours tend to grow faster with increased invasive and metastatic capability and are generally more likely to recur than tumours that do not overproduce HER 2.[2,3] Trastuzumab is the first identified monoclonal antibody designed specifically to attack this over expressed protein, and is used as a follow-on treatment to chemotherapy.[4] (Monoclonal antibodies are laboratory-engineered proteins that are identical because they are produced by one type of immune cell and they help the body's immune system to fight foreign invaders such as cancer).

HOW TRASTUZUMAB WAS DEVELOPED

Trastuzumab is one of a growing collection of therapeutic antibodies which are designed to interact with and block the activities of disease- causing proteins in the body. The catalyst for the development of Trastuzumab was the discovery that many metastatic breast cancers carry multiple copies of the HER 2 gene, which had previously been shown to cause cancer when introduced into mice.

A breakthrough was made by Dennis Slamon in 1987 when he discovered that the aggressiveness of breast cancer was proportional to the number of extra copies of HER 2 in the tumour cells.[5] This led him to approach the biotechnology company Genentech with a proposal to develop an antibody that specifically interfered with the HER 2 protein.

Over the next 10 years, a series of antibodies were made and many pre phase 1 trials were carried out with them in animal models to verify efficacy. Finally, clinical trials in which the best performing antibody was given to women with metastatic breast cancer showed that the drug was very effective at slowing the progress of the disease. Trastuzumab was approved for release in 1998, and has since helped to extend the lives of many women with advanced breast cancer.

HOW TRASTUZUMAB WORKS

Trastuzumab works by interfering with one of the ways in which breast cancer cells divide and grow. Some breast cancer cells divide and grow when a protein that naturally occurs in the body, known as human epidermal growth factor, attaches itself to another protein, known as human epidermal growth factor receptor 2(HER 2), found on the surface of some breast cancer cells. Trastuzumab blocks this process by attaching itself to the HER 2 protein so that the epidermal growth factor cannot reach the breast cancer cells.[6] This stops the cells from dividing and growing. Like other antibodies, trastuzumab may also attract other immune system cells (natural killer cells monocytes) that kill abnormal cells, causing the tumour to regress.[7] Trastuzumab may also block cellular processes that repair damaged DNA. Therefore, when used in combination with DNA-damaging drugs, trastuzumab has yet another way to kill tumour cells.[8,9]

CLINICAL USES OF TRASTUZUMAB

Trastuzumab only works in patients whose breast cancers over express the HER 2 protein. It appears to have little effect on those that do not.

Advanced Breast Cancer

Trastuzumab is used to treat women with advanced breast cancer. It can also be given to treat men with advanced breast cancer. It can be given in combination with chemotherapy drugs to people with advanced breast cancer. It may also be given on its own to people with advanced breast cancer that have already received at least 2 courses of chemotherapy. In 2002, The National Institute for Health and Clinical Excellence (NICE),[10] which advices doctors on the prevention and treatment of ill health, published guidance on trastuzumab for women with secondary breast cancer and approved its use in particular circumstances.

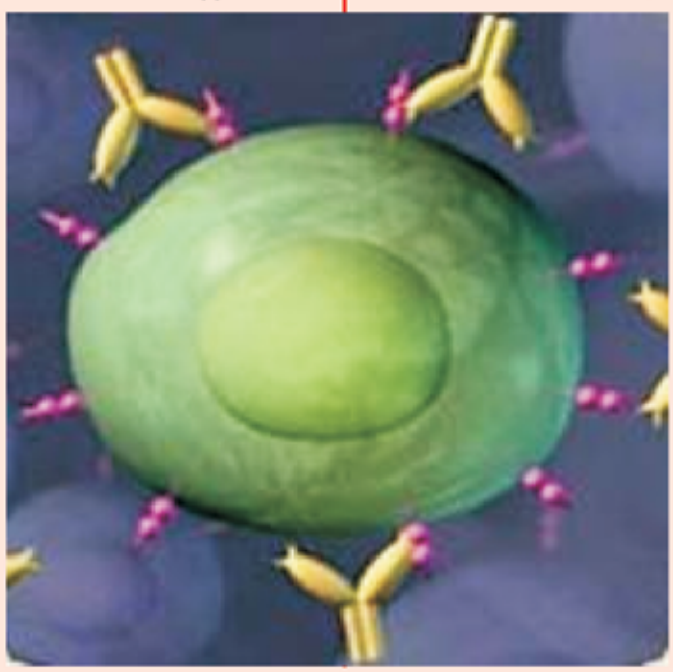
Early Breast Cancer

In the UK trastuzumab was licensed as a treatment for women with early breast cancer in early 2006. It is also given to treat men with early breast cancer although less is known about the potential benefits and possible side effects when it is given to men.

The National Institute for Health and Clinical Excellence (NICE), produced guidelines on the use of trastuzumab in early breast cancer in June, 2006. The guidelines state that trastuzumab should be considered as a possible treatment for women with HER 2 positive breast cancer following surgery and adjuvant chemotherapy (and radiotherapy if appropriate). It recommends that trastuzumab be given every three weeks for one year.[11]

Other Possible Uses

Trastuzumab is undergoing clinical trials for other types of cancer, including osteosarcoma, and cancers of the endometrium, colorectum, kidney, pancreas, prostate, ovary, salivary gland, lung and bladder. All of these tumour types can over express the HER 2 protein on their surfaces.[1]



HOW TRASTUZUMAB IS GIVEN

Trastuzumab is given by a drip (infusion) through a fine tube (cannula) inserted into a vein. The first dose (4mg/kg) is given slowly, usually over an hour and a half. After this, doses (2mg/kg) normally take about 30 minutes.[12] The drug may be given once a week or once every 3 weeks depending on the indication (Advanced or early breast cancer respectively).[10,11]

SIDE EFFECTS

The most severe side effects seen with this drug are heart and lung problems, which tend to occur most often in patients with a history of heart or lung disease. The use of anthracyclines and cyclophospamide in combination with trastuzumab also appears to increase these types of side effects.[13]

The most common side effect with trastuzumab are infusion-associated symptoms, usually consisting of fever and chills on first infusion. The symptoms are often mild to moderate in severity and are treated with Paracetamol, diphenhydramine, and/or pethidine. Other common side effects include nausea and vomiting, and pain (in some cases at tumor sites), which occur less often after the first dose. Lowered red blood cell count (anaemia), lowered white blood cell count (leucopoenia), diarrhoea and infection occur more often in patients receiving trastuzumab plus chemotherapy as compared to chemotherapy alone. The severity of these symptoms usually does not result in discontinuation of therapy with trastuzumab.

Other less common side effects are headache, abdominal pain, back pain, flu-like symptoms, sinusitis, rhinitis, pharyngitis, fluid retention (edema), insomnia, dizziness and depression.[14]

LIMITATIONS TO THE USE OF TRASTUZUMAB IN NIGERIA

1. HER 2 testing: This is done using immunohistochemical staining for the HER 2 protein on the surface of the breast cancer cells or fluorescent in-situ hybridization (FISH) for the HER 2 gene. These tests are not readily available in Nigeria so that samples have to be sent abroad for the tests to be performed. (HER 2/neu testing has been introduced in Nigeria at UCH Ibadan as a research tool. It is still being validated. It is yet to have any impact on clinical management of breast cancer).

2. Cost: Each vial (440mg) of trastuzumab provides treatment for one to three patients, and each vial costs about

S2,300.[15] This means that a patient has to pay approximately S2,300 (About ₦300,000) every 3 weeks for one year to receive treatment with trastuzumab. This cost is extremely high for an average Nigerian to afford.

CONCLUSION

After undergoing several clinical trials for breast cancer that over expresses HER 2, trastuzumab has proved to be effective in preventing recurrence after surgery and in slowing the progress of the disease. The side effects appear to be mild because trastuzumab works specifically on breast cancer cells and does not affect normal cells though precautions have to be exercised when using trastuzumab to treat patients with existing heart and lung problems and during pregnancy and nursing. Trastuzumab also shows future prospects in treating other cancers that over express the HER 2 protein as clinical trials have begun to confirm this.

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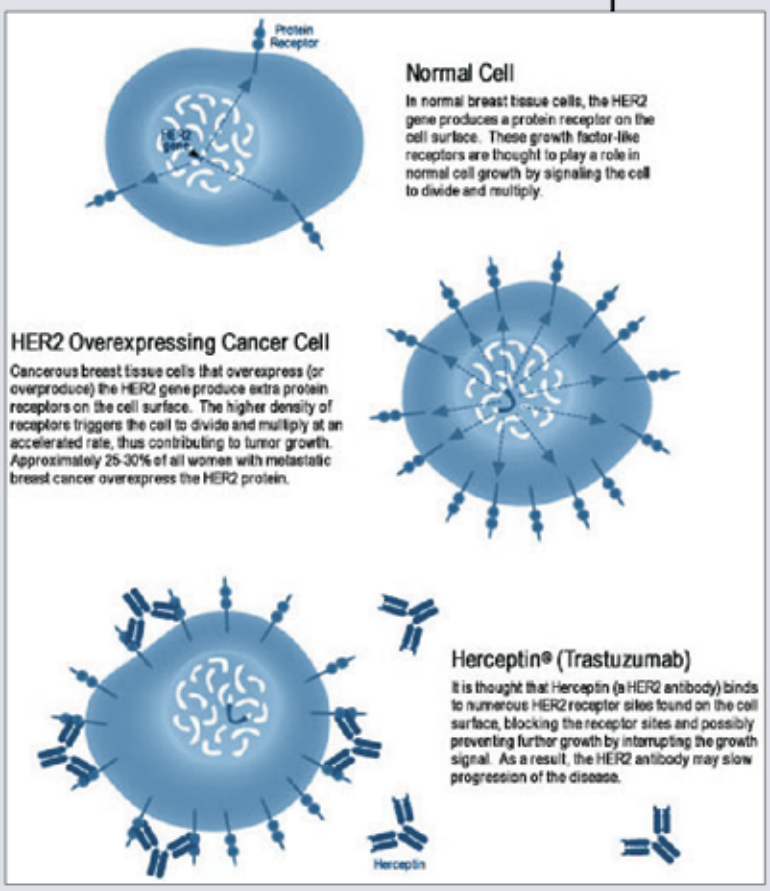

Key words for indexing: TRASTUZUMAB, HERCEPTIN, BREAST CANCER

THE ROLE OF HYSTEROSALPINGOGRAPHY IN THE ASSESSMENT OF INFERTILITY

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ABSTRACT

Hysterosalpingography is the Gold-Standard and cost effective method of assessment the integrity of the female genital tract. It questions the state of the uterus and the fallopian tubes gives a clean bill of health or reveals the disease process afflicting the uterus and fallopian tubes precisely.

Hysterosalpingography utilizes a contrast media either water soluble or oil soluble contrast media which is injected into the uterus via the canula inserted in the cervical canal, and under fluoroscopic vision, spot radiographic films are obtained after a thorough fluoroscopic screening. This procedure must be aseptic.

The patient is usually book for the examination to rule out possibility of pregnancy, menstruation and acute pelvic inflammatory disease which can spell doom for the patient and her doctor.

The major indication for hysterosalpingography is infertility. Hysterosalpingography should only be performed and supervised by a radiologist who is legally liable for the outcome of the examination which at times can be dicey.

The radiologist will deal with the myriads of complications that might result from the examination ranging from mild contrast reaction to cardio-respiratory collapse which could be life-threatening.

The radiologists owe to the patient the duty to explain and convey his findings to the patient via her gynaecologist through a proper and thorough radiologist's report. The radiologist's report is a sacred document. The review article emphasized that hysterosalpingography can also be therapeutic and cited evidence of patients who conceived after the procedure. The radiologists caps it by offering after care to the patient.

INTRODUCTION

Hysterosalpingography is a radiologic procedure where radiographs are taken of a female reproductive tract after injection of a suitable contrast media via canula inserted in the cervical canal. The resulting radiographs obtained after the injection of contrast media depicts the uterine cavity, fallopian tubes and possible free spillage of contrast media into the peritoneal cavity if the tubes are patent.

Hyspero means uterus and salpingo means tubes, so hysterosalpingography literally means radiographic demonstration of the uterus and fallopian tube.

Hysterosalpingography (HSG) is invaluable in the investigation of female infertility, specially in assessing tubal and uterine factors1. Infertility is the commonest complaint encountered in the gynaecological out patient clinics in Nigeria.2 Ojo (1970), reviewing the problem of infertility in Nigeria, concluded that the major single factor responsible for infertility is chronic pelvic inflammatory disease2. Infertility is generally defined as the inability of a couple to conceive within a certain period of time, usually 1 year3.

Infertility can be divided into primary and secondary types. Primary infertility applies to those who have never conceived in their life time whereas secondary infertility which is commoner refers to those who have conceived at some time in the past regardless of whether the pregnancy ended in abortion.

The prevalence of infertility ranges from 7-28% depending on the age of the woman.3 This prevalence rate is high. However with widespread use of Hysterosalpingography (HSG) as a basic radiologic tool and its increasing availability in our country, there is a high probability of making accurate diagnoses of infertility which will lead to prompt treatment where possible and this will in a long run bring down this high prevalence rate.

This article review is aimed at highlighting the indications, contra-indications, preparation/technique, diagnostic finding, complications after care and thereapeutic value of Hystercsalpingography.

INDICATIONS FOR HYSTEROSALPINGOGRAPHY

The major indication for hysterosalpingography is in the assessment of:

1) Female infertility aimed at assessing tubal and uterine factors.1,4,5,6,7
2) Confirmation of tubal patency or the monitoring of tubal patency or occlusion after surgical procedures.6,7
3) Demonstration of congenital abnormalities or other lesions in patients with recurrent abortion.6
4) Assessment of proximal tubal segment before tubal ligation reversal
5) Amenorrhea unresponsive to hormonal stimulation
6) Evaluation of uterine cavity after metroplasty
7) Evaluation of tubal patency after tubal surgery.7
8) Fibroid uterus

9) In staging and grading of uterine synechiae.

CONTRAINDICATIONS OF HYSTEROSALPINGOGRAPHY

Hysterosalpingography is contraindicated during menstruation and pregnancy. Other contra-indications include pelvic sepsis, a recent dilatation and curettage, severe cardiac or renal disease, uterine malignancy i.e. endometrial carcinoma and sensitivity to contrast media.6

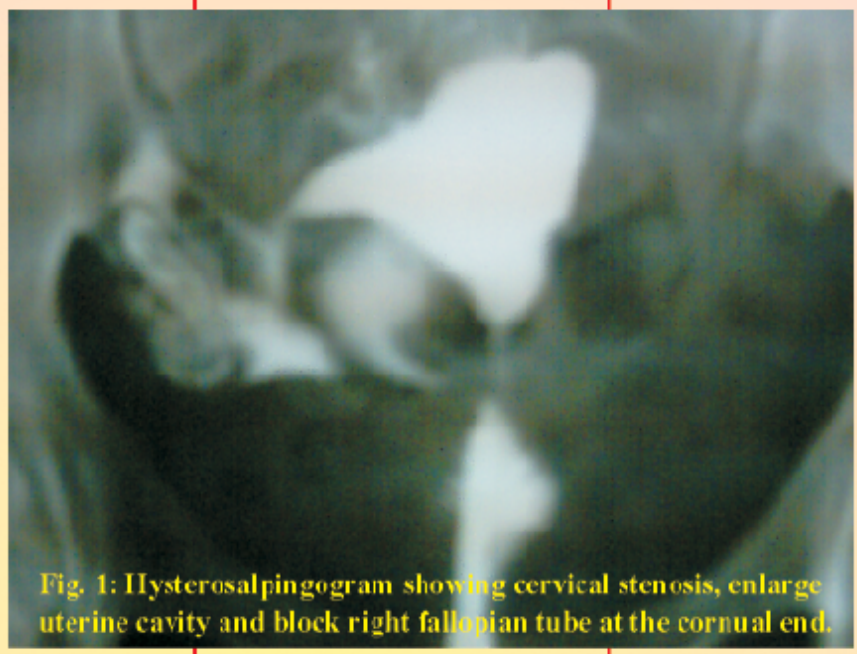

Fig. 1: Hysterosalpingogram showing cervical stenosis, enlarge uterine cavity and block right fallopian tube at the cornual end.

PREPARATION/TECHNIQUE FOR HYSTEROSALPINGOGRAPHY

The preparation for hysterosalpingography commences with a detailed history taking emphasizing on the woman's reproductive history aimed at identifying predisposing risk factors associated with infertility.

These predisposing risk factors include history of septic abortion, use of intra-uterine contraceptive device, pelvic inflammatory disease, appendicitis, ectopic pregnancy, tubal or other abdominopelvic surgery etc.7

After taking the woman's reproductive history, a detailed clinical pelvic examination is the next step to take before scheduling a woman for hysterosalpingography. The pelvic examination is used to evaluate the patient for pelvic tenderness which would suggest pelvic inflammatory disease, clinical pelvic assessment is also utilized to evaluate the position of the uterus eg. anteverted or retroverted and to rule out pelvic mass. Patients with history of pelvic infection should receive tetracycline 100mg twice daily for five days, beginning 2 days before the procedure.7

Hysterosalpingography is usually performed about the middle of the menstrual cycle, after the last day of menstrual flow and before the expected day of ovulation.6,7

Very anxious patients are usually given Diazapam injection 10mg intravenously Buscopam injection, 20mg start and analgesics i.e. Pentazocine 20mg intramuscularly start to minimize discomfort resulting from uterine/tubal sapsm and peritonial irritation by contrast media.

TECHNIQUE

The patient must be booked for the examination according to 10-day rule to avoid performing the examination in a pregnant patient or during active menstruation. Hysterosalpingography is an out-patient radiologic procedure under fluoroscopic guidance by a radiologist, with spot films taken at different intervals during the examination. The total fluoroscopic exposure is usually kept to 30 seconds to minimize radiation exposure to the radiologist.

As with other types of pelvic examinations, the woman will lie on her back on a radiographic table with her legs sometimes raised in stirrups. The x-ray equipment is placed above the abdomen and the central beam centred at the mid-point of the line drawn from the anterior-superior iliac spine and the pubic symphysis in the mid-line or mid-point between the pubic symphysis and the umbilicus.

A bi-valve speculum is inserted into the vagina and opened to expose the cervix. A special hysterosalpingography canula or a paediatric self retaining catheter is used to inject about 10ml of contrast media piece-meal under fluoroscopic vision by the supervising radiologist.

As the contrast media usually urografin which is an ionic contrast media commonly used by radiologists including the author, spreads through reproductive tract the radiologist screens for tubal blockages or other uterine abnormalities fluoroscopically.

Commonly, three spot film are taken accompanied by a scout film obtained before instillation of contrast medium. The cost of hysterosalpingography in Nigeria is between N3000 N10,000.

FINDINGS:

Hysterosalpingography may show normal findings, which will show a healthy, normally shaped uterus and unblocked fallopian tubes which permits egress of free inverted comma shaped contrast spillage into the peritoneal cavity bilaterally.

Hysterosalpingography findings include intra-uterine filling defects, congenital uterine anomalies (Mullerian anomalies), tubal disease such as proximal, middle or distal tubal occlusion with or without hydrosalpinx, endometrosis, salpingitis isthmica nodosa, T-

THE CURRENT TREND IN THE CLASSIFICATION AND MANAGEMENT OF DIABETES MELLITUS IN PREGNANCY

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Summary

Diabetes mellitus is a common medical complication of pregnancy. Its classification has been reviewed to reflect the various aetiological factors. Diagnostic value of fasting plasma glucose has also been reviewed downward to mark the point at which the prevalence of microvascular complications of diabetes mellitus increase dramatically. Preconception care, early antenatal booking, dedicated multidisciplinary antenatal care, and delivery in a center with neonatal facility would reduce morbidity and mortality associated with the condition. Glibenclamide is considered safe after the first trimester and it gives comparable result to insulin therapy.

Key Words: Diabetes mellitus, pregnancy, diagnosis, preconception, antenatal, delivery, oral hypoglycaemics.

Aim of the review

There are lots of controversies surrounding diabetes mellitus in pregnancy.[1] This review hopes to highlight the current position in the classification, diagnosis and treatment of diabetes mellitus in pregnancy. This would help clinicians improve their patients' management based on current thinking/evidence.

Definition

Diabetes mellitus is a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia with disturbances of carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action, or both.[2]

Classification

Pre-gestational Diabetes Mellitus: This is Diabetes mellitus that antedates pregnancy. It is referred to as *Diabetes Mellitus and pregnancy*[2] and is sub classified according to aetiology into types 1 and 2. The use of terms *Insulin Dependent Diabetes Mellitus* (IDDM) *and Non Insulin Dependent Diabetes Mellitus* (NIDDM) has been eliminated because they are confusing and they are based on treatment instead of pathogenesis.[2]

Type 1 Diabetes Mellitus is due to pancreatic islets beta-cell destruction, usually autoimmune. It was formally referred to as *Insulin Dependent Diabetes Mellitus (IDDM)*. Type 2 Diabetes Mellitus is due to insulin resistance. It was known *as Non-Insulin Dependent Diabetes Mellitus (NIDDM)*. Because of presence of insulin, they are not ketosis-prone unlike Type 1 diabetics.

Gestational Diabetes Mellitus (GDM): Gestational diabetes is carbohydrate intolerance of varying severity with onset or first recognition during pregnancy.[3] It does not exclude the possibility that the glucose intolerance may antedate pregnancy but has been previously unrecognized. The definition applies irrespective of whether or not insulin is used for treatment or the condition persists

after pregnancy.[2]

Prevalence

Worldwide prevalence of diabetes in pregnancy is 3 7 per 1000 pregnancies.[4,5,6] Of these, about 90% are classified as GDM, 7% are previously diagnosed type 2 diabetes, and 4% are type 1 diabetes.[6] In Nigeria, prevalence of Diabetes mellitus in pregnancy varies but are generally less than 3 per 1000 deliveries.[7,8]

Screening for Gestational Diabetes mellitus (GDM)

Screening for GDM can be Selective or Universal (Routine) depending on the setting.[9,10] It selective in University of Nigeria of Nigeria Teaching Hospital (UNTH), Enugu, Nigeria.
Selective screening is recommended as soon as feasible for women at risk and should be repeated between 24 28 weeks of gestation if results of testing do not demonstrate diabetes.[11] Risk factors for screening include past obstetric history of macrosomic baby (ies), gestational diabetes mellitus and, unexplained perinatal death(s). Others are family history of diabetes mellitus, maternal age above 35years, estimated fetal weight greater than 4kg, polydipsia, polyuria, polyhydramnious, repeated or heavy glycosuria, and maternal obesity. However, a study In Ibadan, Nigeria, showed no statistical difference in the incidence of overt diabetes mellitus and GDM between obese women and the control.[12] All screening guidelines for GDM are based on level III evidence.[1] This may not be unrelated to the observation that some centers and specialists neither screen nor treat GDM.[11] Furthermore, some clinicians challenge the existence of GDM[14] and this is supported by a report in *the Cochrane Library* showing no evidence that screening or treatment of GDM, made an appreciable difference in perinatal outcomes.[15]

The above exposes the uncertainties surrounding this clinical entity. However, since obstetrics is a high-risk part of practice, it makes sense that, until GDM is universally declared benign, we need to screen and treat.[1]

Screening/diagnosis of GDM

The following methods can be used to rule-out or rule-in gestational diabetes mellitus depending on the plasma glucose level obtained. The methods and their accompanying normality and diagnostic values are shown below. Individuals with plasma glucose values in between normal and diagnostic ranges should be subjected to 75g 2-hr Oral Glucose Tolerance Test (OGTT) [2] or 100g 3-hr OGTT.[16]

- 50g non-fasting 1hr glucose challenge: This is the gold standard.[3]
  <7.8mmol/l (140g%) = normal
  >=10.3mmol/l (185g%) may be considered diagnostic of DM.[17]
  7.8 10.2mmol/l requires Oral Glucose Tolerance Test (OGTT).
- Random Plasma Glucose:
  <7mmol/l = normal
  >=11.1mmol/l = DM
  7 11mmol/l requires OGTT
- Fasting Plasma Glucose:
  4 6mmol/l = normal
  >=7.0mmol/l (126g%) = Diabetes mellitus[2]
  5.1 6.9mmol/l requires OGTT
- 2-Hour Plasma Glucose (2-HPP):
  <9mmol/l = normal
  >=11.1mmol/l (200mg%) = Diabetes mellitus
  9 11mmol/l requires OGTT.

The diagnostic value of fasting plasma glucose of greater than or equal to 7.0mmol/l marks the point at which the prevalence of microvascular complications of diabetes mellitus (retinopathy and nephropathy) increase dramatically.[2]

Fasting plasma glucose in combination with 2-Hours Post Prandial (2-HPP) is the method mostly used in UNTH, Enugu for screening and diagnosis of GDM. For clinical purposes, the diagnosis of diabetes mellitus using these should be confirmed on a subsequent day, and precludes the need for OGTT.[4,11,18]

Oral glucose tolerance test (OGTT)

Venous plasma glucose	100g OGTT (mmol/l)	75g OGTT (mmol/l)
Fasting	5.3 (95g%)	5.5 (95g%)
1-hour	10.0 (180)	10.0 (180)
2-hour	8.6 (155)	8.6 (155)
3-hour	7.8 (140)	Not indicated

Two or more of the venous plasma concentrations in OGTT must be met or exceeded for positive diagnoses. Sensitivity of OGTT is 80% while the Specificity is 85%.[7] One abnormal OGTT result is associated with fetal macrosomia and when such women undergo repeat OGTT, 1/3 will demonstrate a positive diagnoses.[19]

Fasting Blood Sugar (FBS) alone when compared with OGTT, has similar sensitivity (80%) but high false positive rate (specificity 57%).[20] The specificity improves when combined with 2 HPP.

Preconception care

This is necessary for pre-gestational Diabetes mellitus. Pregnancy should be planned. Aim of preconception care is to maintain blood sugar within normal level because periconceptual hyperglycaemia is teratogenic.[21] Oral hypoglycaemics are converted to insulin therapy. Attempts should be made to rule out and/or access extent of complications such as retinopathy, and offer appropriate counseling or treatment.

In addition, folate supplementation should be offered, and the woman counseled on the need for socio-economic preparation for pregnancy and childcare.

Antenatal management

Management involves Diet and/or Insulin, Exercise, and Education[11]. She should be encouraged to register early in a dedicated diabetic antenatal clinic staffed by an obstetrician with special interest in diabetic pregnancy, a diabetologist, a diabetic nurse/midwife, and a dietician.[4,19,22] She should be admitted at booking (for Pre-gestational DM) or at diagnosis of GDM for stabilization.[22]

Initial treatment is dietary. Insulin should be commenced if initial FBS is greater than or equal to 8mmol/l, or when the FBS is consistently greater than 6mmol/l despite diet therapy.[5]

Antenatal visits should be more frequent[4] and where indicated, twice daily or four times daily insulin with combinations of regular and intermediate/ long acting preparations give good and comparable results. Blood glucose checks should be carried out many times (4 6) per day. Anomaly ultrasound scan should be carried out between 18 and 22 weeks of gestation.

Fetal surveillance is necessary in third trimester and serial Biophysical profile (BPD) is of great value.[1] Finally, delivery plan should be formulated at 36 weeks gestational age.[4]

Delivery

Spontaneous vaginal delivery should be the method of choice for all women with diabetes, wherever possible. For well-controlled cases and uncomplicated pregnancy, it should be possible to reach 39 completed weeks of gestation .[4,11,22] Beyond this, there is little evidence of benefit and some evidence of harm.[1] Poorly controlled diabetes mellitus may require earlier delivery however, amniocentesis for fetal lung maturity assessment may be necessary.[19]

During labour or Cesarean section, euglycaemia is maintained with infusion dextrose and sliding scale of insulin administration[5,19] or with Glucose/Potassium/Insulin (GKI) Infusion. Adequate analgesia is required during labour or cesarean section for good glucose control.[4] Pain elaborates catecholamines, which impair plasma glucose control. Post cesarean section, ensure good wound care and early ambulation.[22]

Postnatal care

Insulin requirement falls by half within 24 hours of delivery then, by further one quarter if the woman breastfeeds .[11] Adequate adjustments of insulin therapy are therefore necessary. Contraceptive counseling should be offered: barrier methods, Mini-pills, low dose Combine Oral Pill, and IUCD are safe.[4,11] Sterilization should be encourage if patient has completed her family.

At six weeks postnatal visit, GDM patients should be subjected to a repeat OGTT following which they should be reclassified accordingly.[3,19]. Afterwards, she should be referred to appropriate clinic(s) as necessary such as medical diabetic clinic, and family planning clinic.

Oral hypoglycemic and diabetic pregnancy

In 1994, placental testing demonstrated that glibenclamide (glyburide), a second-generation sulfonylurea, did not cross the placenta.[23] No randomized controlled trials have focused on use of oral hypoglycemics during organogenesis during the first trimester.[1] When glibenclamide is used for DM in the second and third trimesters (beginning at 11 weeks' gestation), their outcomes were similar to those randomized to insulin treatment, and there was no risk to mother or fetus.[24] A survey of American obstetricians indicated that 13% of them begin treatment of GDM with glyburide when diet and exercise fail.[25]

Furthermore, studies of placental transportation of metformin and umbilical cord analyses in metformin-treated patients have not been done recently.[1] However, non-diabetic women with Polycystic ovary syndrome treated preconceptually and throughout pregnancy with metformin had a lower incidence of GDM and produced healthy, normal infants.[26,27]

It is possible that the teratogenic effects attributed to oral hypoglycaemics may be due to hyperglycaemia. More research is therefore required in this area.

Conclusion

Management of diabetes in pregnancy remains a controversial issue in obstetrics. Clinicians should open their minds to newer classifications and treatments such as use of oral hypoglycemics, in line with current evidence in the interest of patients. Adequate female education and empowerment as well as improvement of quality of services obtainable in our hospitals are still very necessary for good female reproductive health in general, and management of diabetes in pregnancy in particular.

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Case 2

U.N, a 20 year old female student of a college of education was brought to the emergency department of the hospital in September 2003 by her mother who reported her daughter as having developed difficulty in opening her mouth since five days earlier. This was followed two days later by generalized spasm of the limbs, which were precipitated by noise. The mother had no other relevant informant to offer except that her daughter was resident in the school's hostel and had come back home a week earlier complaining of fever and a sore throat; symptoms she seemed to have suffered a bit too often in the last two months.

On examination the patient was pyrexic (38.2) but otherwise conscious and alert. She had marked trismus with rigidity of abdominal, trunk and limb muscles. Provocation yielded generalized spasms of 5s 10s duration involving the neck, trunk and limbs. A few upper cervical lymph nodes including the jugulo-digastric were found to be mildly enlarged and non-tender.

A diagnosis of tetanus of yet unknown source was made. Her management consisted of routine intravenous fluids, nasogastric tube feeding, spasm control (using a combination of chlorpromazine, diazepam and phenobarbitone) and other conservative measures. A neutrophil leucocytosis of 11,000/mm^3 was picked up by the second day of admission. Other investigations were normal. The fever responded to intravenous ciprofloxacin.

By the tenth day of admission of the patient, now reasonably well recovered volunteered on discrete questioning that she acquired a new lover who preferred oral sex performed on him. In the last few weeks she had experienced sore throat after each sexual encounter, the last being a week before the onset of her symptoms. Inspection of the buccal mucosa revealed some erosions, obviously healing on the posterior pharyngeal wall. She claimed these had been painful ab initio. Further diagnostic work-up was hampered by financial handicap and the patient as counseled on the danger of continuing oral sex with her friend She was discharged and lost subsequently to follow-up.

DISCUSSION

The commonest source of infection in tetanus is the wound sustained by stepping on dirty nails or wood/ thorns.[3, 6] This makes the initial care of wound treatment and post wound tetanus prophylaxis very important. In the rural communities of Africa tetanus commonly results from wounds sustained on the farms from thorns while walking bare foot or from cutlass cuts from fights.

In as many as 20% of patients, it is not possible to identify a possible source of infection or portal of entry.[1] The doctor working in a busy medical service may not consider it very rewarding to keep revisiting a patient's history. Here are two cases, one following a human bite wound sustained in a jealous fight and the other following exposure to oral sex and pharyngeal ulcers from a probable sexually transmitted disease. These cases highlight the wide spectrum of possible portals of entry for tetanus in a developing country like Nigeria. Bite wounds are uncommonly encountered as having resulted in tetanus. Some cases have been reported to follow animal bites[5] but we were unable to find a documented case in the literature of tetanus secondary to a human bite.

Sexual preferences particularly among the youthful population in societies hitherto classified as being traditional, conservative and non-deviant are rapidly changing. Globalization has resulted in sexual practices more commonly encountered in western countries gaining adherents in these other societies. We have not also come across a report in the literature of tetanus resulting courtesy of a sexually transmitted disease.

It is important for clinicians to be comprehensive in their approach to every case of tetanus and to have a high index of suspicion particularly in cases with no obviously perceived portal of entry.

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KEROSENE POISONING IN A CHILD

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Keywords: Kerosene , Poisoning, Children, Pneumonitis,

Abstract

Kerosene poisoning is common in modern society especially in the pediatric age group and in communities where kerosene is a major household fuel. The exact incidence of kerosene poisoning in Nigeria is unknown. Generally cases are under reported as some patients are asymptomatic. The circumstance is usually that of accidental ingestion of kerosene probably mistaken for water. Kerosene, a petroleum distillate hydrocarbon is a central nervous system depressant, a gastrointestinal and respiratory irritant poorly absorbed after ingestion but absorption following inhalation or pulmonary aspiration is rapid. Aspiration into the lungs may occur with ingestion or as a result of vomiting and cause pneumonitis.

This is the case of a 2 year old girl who was brought to the children emergency room of UNTH Enugu with altered consciousness and noisy breathing following kerosene ingestion. Following treatment she made an excellent recovery and was discharged 3 days later

CASE REPORT

NK, a 2-year old girl was brought to the Children Emergency Room CHER of the University of Nigeria Teaching Hospital on March 6, 2006 with a history of altered consciousness and noisy breathing following kerosene ingestion. According to the mother, the child was found lying in a pool of kerosene on the kitchen floor. Further questioning revealed that the child was coughing and choking with a noisy breathing. She had a non-projectile vomiting 5 minutes later. The vomitus was small in quantity and consisted of clear fluic. The mother confirmed that both the vomitus and the child's breath smell strongly of kerosene; and that the kerosene was contained in a 350ml plastic container, which was lying empty on the floor beside the baby. On their way to hospital, the baby had one episode of seizure. The seizure which was of generalized tonic clonic nature lasted for 5 minutes. On examination at CHER, NK was comatose with a Glasgow coma scale of 8. Her mucous membranes were pink, she was acyanotic, anicteric, well hydrated and febrile with an axillary temperature of 38.6°C. Evaluation of the central nervous system revealed an unconscious child with normal sized pupils that were symmetrical and reacted to light. Other cranial nerves were intact with no detectable meningeal signs. Muscle bulk was normal, power was 3/5 in all the limbs with an increased tone globally and exaggeration knee jerk reflexes. Respiratory examination revealed a child in obvious respiratory distress and wheezing. Respiratory rate was 35 breaths/minute and there was rhonci on auscultation of both lung bases.

Examination of other organ systems showed no abnormality. Based on a strong history of kerosene ingestion and abnormal CNS and respiratory findings, a diagnosis of kerosene poisoning was made. She made an uneventful recovery following treatment with supplemental oxygen after airway had been secured, and was maintained on intravenous fluid, 5% dextrose in 0.45% saline. She was also commenced on broad spectrum antibiotics(IV cefuroxime 100mg/kg/day).

DISCUSSION

Exposure to Kerosene is common in modern society. In Nigeria Kerosene is the major household fuel; being derived from petroleum distillates, it is one of the most dangerous hydrocarbons. Types of exposure include accidental ingestion, dermal contact or oral ingestion in a suicide attempt. The highest rates of morbidity and mortality result from accidental ingestion by children younger than 5 years.

The toxic effect of kerosene is related to its physical properties, which include high volatility, low viscosity and low surface tension[1]. Highly volatile compound with low viscosity and low surface tension are more likely to be inhaled or aspirated into the respiratory system. Kerosene is poorly absorbed after ingestion but absorption is rapid after inhalation or pulmonary aspiration[2]. Though absorption may be minimal, this also depends on the quantity ingested. Therefore, when large quantity is ingested, more kerosene tend to get absorbed into the general circulation.

Aspiration pneumonitis is the most common complication of hydrocarbon ingestion, followed by central nervous system and cardiovascular complications[3]. Though some cases may be asymptomatic, presentation is mostly of acute respiratory distress, as a result of chemical pneumonitis and bronchospasm. There may be intra alveolar hemorrhage. Respiratory symptoms generally begin in the first few hours after exposure and usually resolves in 2-8 days. Complications include hypoxia, bacterial pneumonia and emphysema. Prolonged hypoxia may result in encephalopathy, seizures and death. Bacterial pneumonia is a result of secondary bacterial infection. Common organisms implicated include Staphylococcus pyogenes, Streptococcus pneumonia, Haemophilus influenzae and gram negative bacilli[3]. These will lead to lobar or bronchopneumonic consolidation, abscess formation and pleural effusion. Emphysema is a long term effect and may follow barotraumas following mechanical ventilation. It is therefore necessary that timely and appropriate treatment be instituted in order to avoid this complications.

Diagnosis of kerosene poisoning can be made even in the absence of specific laboratory parameters if there is a positive history of exposure (ingestion) supported by compatible respiratory and neurological findings. In the patient, the confluence of signs and symptoms along with an identifiable source of kerosene excluded other aetiology and satisfied the criteria for diagnosis.

BIPOLAR AFFECTIVE DISORDER

ABSTRACT

In the Diagnostic Statistical Manual (DSM-IV) adopted by the American Association of Psychiatrists, the essential feature of Bipolar Affective Disorder is the occurance of at least one episode of mania, usually but not necessarily, accompanied by at least one depressive episode. Thus, any previously well person suffering from a first episode of mania (or hypomania) would be classed as suffering from this disorder. If a previously well person suffers from one or more depressive episodes, he or she is not classed thus till an episode of mania occurs.

In the International Classification of Diseases (ICD-10) adopted by World Health Organisation, the definition of Bipolar Disorder is slightly different. There must be a history of at least two episodes of mood disturbances and one of these should be mania (or hypomania). The similarities and differences between the two classification systems are illustrated in Figure I below:

(INSERT FIGURE I HERE)

The psychopathologic Mania Rating Scales were introduced to show the DSM-III and DSM-III-R criteria for mania. These brief Rating Scales represent not diagnostic scales but scales for measuring the severity of this psychopathology. The syndrome of mania is symptomatically scored without reference to aetiologic theories. An indication is given for the corresponding syndrome of the DSM-III-R criteria.

(INSERT RATING SCALES HERE)

This Case Report is that of a 25 year old student/model who presented at Casualty Department of the Enugu Neuropsychiatric Hospital with ten days history of poor sleep and five days history each of talkativeness and over-religiousity prior to presentation, the treatments she received and the remarkable improvement recorded.

INTRODUCTION

Bipolar Affective Disorders are mood disorders in which depression alternates with manic states. Such individuals exhibit extremes of mood with accompanied changes in affect over a period of time.

On presentation, the dominating clinical feature may range from hypomania, mania (with or without psychotic symptoms), depression (mild, moderate or severe with or without psychotic symptoms) or mixed episodes of mania and depression. This forms the basis of its classification by the International Classification of Diseases (ICD).

Clinical manifestations observed include elevation of mood (elation or irritability), high energy, over activity, pressure of speech, lack of sleep, loss of normal social and sexual inhibitions, low attention and concentration. Neglect of eating, drinking and persona. hygiene which may lead to dangerous states of dehydration and self neglect. During a manic episode, a patient may overspend or be inappropriately aggressive and angry.

Mean age of onset is mid-twenties although it can occur for the first time in old age. When occurring in adolescence it maybe mistaken for schizophrenia. Bipolar disorders have been found more commonly in the upper social classes. Sex ratio is equal. Point prevalence of this disorder in Western countries (based on US studies) is between 0.4 and 1% in the general population. The life time risk in general population of Western countries is 0.6-1.1%.

Predisposing factors of mood disorders (both depressive episodes and bipolar disorders) include genetic factors and personality (cyclothymic-cyclical mood changes and cycloid personality disorder). Precipitating factors are psychosocial stressors (recent life events, vulnerability factors) and physical illness (eg viral infection). Perpetuating and Mediating factors are psychological factors (e.g learned helplessness, depressive cognitive triad), social factors (eg lack of a confiding relationship, high expressed emotion). Neurotransmitters (monoamine hypothesis), Psychoneuroendocrinological factors, Water and Electrolyte changes, Sleep changes and Phobic changes.

Patients with mania should be treated as in-patients. Mainstay of treatment of acute (hypo) mania is Anti-psychotic medication. Lithium is used in prophylaxis and Electro-convulsive therapy is used to treat manic stupor. Compliance with prophylactic medication (Lithium and Carbamazepine) leads to a better prognosis of bipolar disorder.

CASE SUMMARY

A 25year old single female final year law student and a model who is a Christian of the Roman Catholic denomination was accessed by a psychiatrist on referal from a prayer ministry.

She was brought by fiance and parents with ten days history of poor sleep and five days history of talkativeness and over-religiousity all prior to presentation.

The psychiatrist noted that there is no history of previous mental disorder in the patient or any member of the family.

She had previously complained prior to the illness of fiance always being away on business trips and not giving her adequate attention and care. Most of her talks centred on religion. Claimed to have healing powers and attempting to lay hands on people that come