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Nigerian Institute of Medical Research is the oldest and the apex medical research institute in Nigeria with mandate (Act of 1977) to conduct research into health problems in the country.

Historical Background

The present Nigerian Institute of Medical Research was established in 1920, with the arrival of a medical team, under the auspices of the Rockefeller Foundation Yellow Fever Commission to the West Coast of Africa. In 1925, another team from the West African Yellow Fever Commission arrived Lagos to join the team from the Rockefeller Foundation and the research facilities at the centre were expanded.

In 1954, the research centre was named the West African Council for Medical Research and in 1960 it metamorphosed into the Medical Research Council of Nigeria. Through the Research Institute Establishment Order of the National Science and Technology Act of 1977, the Medical Research Council of Nigeria was renamed the National Institute of Medical Research. The name was further modified in 1993 to the Nigerian Institute of Medical Research. Nigerian Institute of Medical Research is currently the oldest health research institute in the country.

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Review Articles

Maternal mortality in Nigeria – The way forward

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SUMMARY

According to the 2005 worldwide estimate, developing countries accounted for 99% (533,000) of the estimated 536,000 maternal deaths. Sub-Saharan Africa and South Asia accounted for 86% of global maternal deaths. Nigeria is among the 14 countries with maternal mortality ratios (MMR) of over 1000. The average Nigerian MMR of 1100 is unacceptably high, even by African standards (Ghana: 560, Gabon: 520). The lifetime risk of maternal death in sub-Saharan Africa is 1 in 21; 1 in 18 in Nigeria, 1 in 45 in Ghana and 1 in 53 in Gabon; while it is 1 in 7300 for the developed regions of the world.[6]

The maternal mortality ratio in 1999, by geo-political zones in Nigeria, showed that the northwest (1,549/100,000) and northeast (1,025/100,000) had particularly high ratios. By comparison, the southeast recorded 286/100,000 live births, while the southwest stood at 165/100,000 live births.[10] The MMR in different zones of Nigeria reflects the quality and quantity of health care delivery facilities in each zone of the country.[4] The southwest has the highest number of health care delivery facilities, while the northeast and the northwest have the lowest, with attendant high MMR..

Nearly two-thirds of the maternal deaths worldwide are due to five direct causes: haemorrhage, obstructed labour, eclampsia (pregnancy-induced hypertension), sepsis and unsafe abortion. The remaining one-third are due to indirect causes or an existing medical condition that is worsened by pregnancy or delivery (such as malaria, anaemia, hepatitis, or increasingly, AIDS).

Most of Europe and North America once had levels comparable to those in the developing world today. Their near universal access to skilled attendance at birth and to emergency obstetric care has reduced maternal mortality rates to almost zero.

INTRODUCTION

The tenth revision of the International Classification of Diseases (ICD-10) defines maternal death as the death of a woman while pregnant or within 42 days of the termination of her pregnancy, irrespective of the duration and site of the pregnancy, from any cause related to or aggravated by the pregnancy or its management, but not from accidental or incidental causes.[1] The 42-day limit is somewhat arbitrary and in recognition of the fact that modern life-sustaining procedures and technologies can delay death, ICD-10 introduced a new category, namely, *late maternal death*, which is defined as the death of a woman from direct or indirect obstetric causes after more than 42 days, but less than one year after termination of pregnancy.

According to ICD-10, maternal deaths should be divided into two groups:

Direct obstetric deaths. Those which result from obstetric complications of the pregnant state (pregnancy, labour and the puerperium) from interventions, omissions, incorrect treatment or from a chain of events resulting from any of the above.

Indirect obstetric deaths. Those which result from a previously existing disease or a disease that developed during pregnancy and which was not due to direct obstetric causes, but was aggravated by physiologic effects of pregnancy.

The drawback of this definition is that maternal deaths can escape being so classified, because the precise cause of death cannot be given, even though the fact of the woman having been pregnant is known. Such under-

registration is frequent in both developing and developed countries.

Death from 'accidental or incidental' causes have historically been excluded from maternal mortality statistics. In practical terms, there are two distinct approaches to identifying maternal deaths, one based on medical causes following the ICD-10 definition of maternal death, and the other based on proximity of death relative to pregnancy, that is, using the ICD-10 definition of pregnancy-related death.

Maternal mortality is statistically estimated using three measures. One of the measures is the maternal mortality ratio (MMR), which is the number of maternal deaths during a given time period per 100,000 live births. This is commonly used to measure maternal mortality. Other statistical measures are the maternal mortality rate and the adult lifetime risk of death. The maternal mortality rate is the number of maternal deaths in a given period per 1000 women of reproductive age during the same period. The adult lifetime risk of maternal death is the probability of dying from a maternal cause during a woman's reproductive life span.[2]

Maternal mortality rates and ratios are difficult and expensive to obtain and are often inaccurate. In many poor countries with limited vital registration systems, tracking these numbers accurately is a nearly impossible task. *Process indicators* are easier to track and can be used to show changes in those activities or circumstances that are known to contribute to or prevent maternal death. These indicators have become an invaluable tool to monitor the progress in programme implementation and effectiveness.

Useful process indicators for maternal mortality include the percentage of deliveries with skilled attendants, the number of facilities offering emergency obstetric care (EmOC), their geographic distribution, the percentage of women with complications treated in EmOC facilities, the caesarean section rate and case fatality rates. When taken together, these indicators offer a picture of the availability, quality and use of services. This is, in many ways, exactly the information that programmers need. Impact indicators such as maternal mortality rates and ratios remain a useful measurement, especially in making international comparisons. The indicator selected to measure progress against the Millennium Development Goals is the proportion of births attended by a professionally-trained and skilled attendant. Other common indicators used to monitor and evaluate safe motherhood include the percentage of pregnant women attending antenatal care at least once during their pregnancy and the percentage of women receiving postnatal care.[3]

The MMR in the different zones of Nigeria reflects the quality and quantity of health care delivery facilities in each zone of the country.[4]

The factors which contribute to high risk behaviour is the low status of women, poverty, ignorance, illiteracy and harmful traditional practices, as well as religious beliefs that act as barriers to the utilization of available health services.

The current practice of some religious sects of taking deliveries in churches/mission houses without the appropriate personnel also contributes to the high MMR in Nigeria.[5]

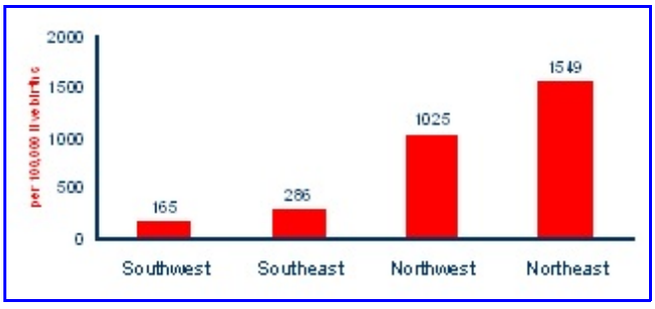

Figure 1. Maternal mortality ratio by zone, Nigeria.

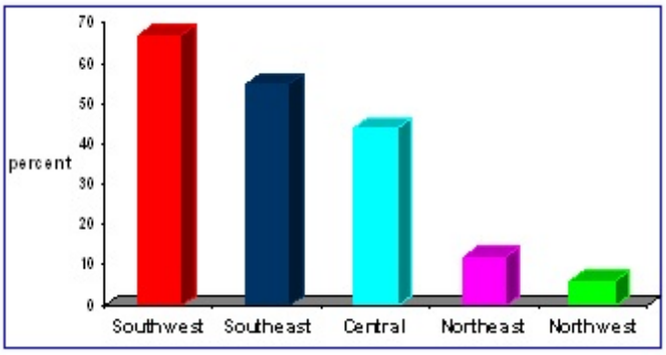

Figure 2. Percentage of women who delivered with skilled birth attendants.

The southwest has the highest number of health care delivery facilities; the areas with the lowest number of health care facilities is the northeast and the northwest, with resultant higher MMR.

Only 37% of deliveries in Nigeria were attended by skilled birth attendants (nurse/midwives and doctors). High risk fertility behaviour is also common in Nigeria as shown in figure 3.

MAGNITUDE OF THE PROBLEM

The developing countries accounted for 99% (533,000) of the estimated of 536,000 maternal deaths worldwide in 2005. Slightly more than half of the maternal deaths (270,000) occurred in sub-Saharan Africa, followed by South Asia (188,000). Thus, sub-Saharan Africa and South Asia accounted for 86% of global maternal deaths.[6] The MMR was highest in the developing regions (450 maternal deaths per 100,000 live births), in stark contrast to developed regions (9) and countries of the commonwealth of independent states (51). Among the developing regions, sub-Saharan Africa had the highest MMR (900), followed by South Asia (490), Oceania (430), Southeast Asia (300), West Asia (160), North Africa (160), Latin America, and the Caribbean (130) and East Asia (50).[6]

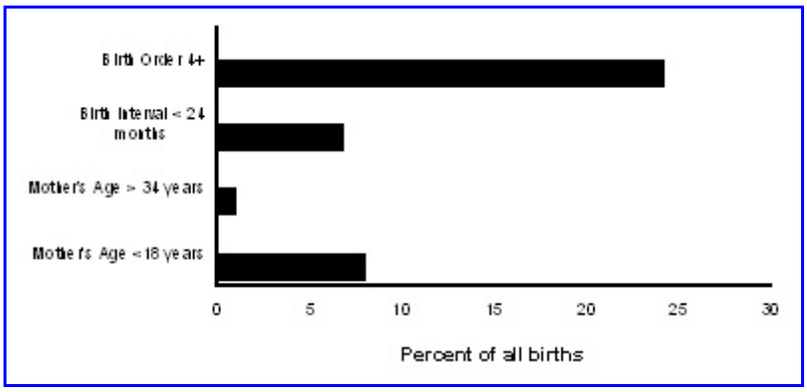

Figure 3. High risk fertility behaviour in Nigeria

Nigeria, with an MMR of 1100, was among the 14 countries with MMRs over 1000. This is unacceptably high, even by African standards (Ghana: 560, Gabon: 520). The lifetime risk of maternal death in sub-Saharan Africa is 1 in 21; 1 in 18 in Nigeria, 1 in 45 in Ghana and 1 in 53 in Gabon, while it is 1 in 7300 for the developed regions of the world.[6]

Nigeria had the second highest number of maternal deaths in the 2005 estimated at 59,000. This was second only to India, with 117,000, while Democratic Republic of Congo (DRC) was third with 32,000. Nigeria, therefore, accounts for 11% of global maternal mortality, while it makes up only 1.76% of the world's population.

Studies from several parts of the country have alluded to the continuing high maternal mortality ratio.[7,8,9] The maternal mortality rates in 1999, by geo-political zones in Nigeria, showed that the northwest (1,549/100,000) and northeast (1,025/ 100,000) had particularly high rates. By compari-son, the southeast recorded 286/ 100,000 live births while the southwest stood at 165/100,000 live births.[10] The high ratio of maternal mortality in the developing countries has been a major source of concern to all stakeholders. In an attempt to reduce maternal mortality, the United Nations included the reduction of maternal mortality by 75% by the year 2015, as one of its health-related millennium development goals. Current trends, however, suggest that in Africa, this objective may not be achieved.[11]

The persistent high rate of maternal mortality in Nigeria calls for a periodic reappraisal so as to identify potential areas of possible intervention aimed at reversing this trend.[12]

In addition to these deaths, hundreds of thousands sustain serious short and long-term morbidities, some of which are quite debilitating. It is estimated that for every maternal death, about 20 other women suffer serious pregnancy-related morbidities. These include: infertility, anaemia, chronic pelvic pain, dysmenorrhoea and injury to the reproductive organs, e.g. fistulae, perineal tears, symphyiolysis.[13-19] Maternal death is only the tip of the iceberg of health consequences women suffer in the course of fulfilling their biological role of procreation in Africa.[20]

CAUSES OF MATERNAL MORTALITY

Nearly two-thirds of maternal deaths worldwide are due to five direct causes: haemorrhage, obstructed labour, eclampsia (pregnancy-induced hypertension), sepsis and unsafe abortion. The remaining one-third are due to indirect causes or an existing medical condition that is worsened by pregnancy or delivery (such as malaria, anaemia, sickle-cell disorder, hepatitis, AIDS). About 15% of all pregnancies will result in complications. If untreated, many of these complications will be fatal. What makes maternal mortality such a challenge is the fact that these complications are extremely difficult to predict. While the general health status of pregnant women is important for a positive outcome of delivery, deadly complications randomly occur in all women. This is the case even in the developed world, where the latest medical technology is readily available. Prediction is generally limited to identifying only high-risk groups of women. It is nearly impossible to determine which particular woman will develop complications. In reality, the overwhelming majority of pregnancies and births take place among women who are considered low risk.[3] Consequently, while the percentage of deaths may be higher among

high-risk women, the greatest number of deaths take place among women considered to be low-risk.

The underlying medical causes of maternal mortality are contributory or predisposing factors which can be divided into sociocultural, reproductive and health services factor.

The sociocultural and economic factors include poverty, low economic status of women, poor nutrition, illiteracy and ignorance, religious beliefs that prevents utilisation of available health care services and harmful traditional practices.[21]

The reproductive health causes of maternal mortality include pregnancy at the extremes of age, ie, pregnancy at less than 15 or older than 35 years of age, grand multiparity, lack of adequate spacing between pregnancies, and pregnancy during serious maternal medical illnesses. Other factors include unsafe abortion, the high prevalence of malaria, the high rate of malnutrition and the HIV/AIDS pandemic.

The Nigerian health services also contribute to the high maternal mortality rate. Most communities in the rural areas do not have access to essential obstetric care (EmOC) or family planning services. The majority of health care facilities lack safe water, electricity, basic life-saving equipment, blood, and various consumables to deal with emergencies. The number of skilled birth attendants is insufficient to maintain a 24-hour service. Most primary health care centres do not have an efficient referral network, as they lack communication and transportation.

A framework to explain the social factors responsible for many maternal deaths can be summed up with one word: 'delay'. In most instances, women who die in childbirth experienced at least one of the following three delays:[22]

- **The first delay** occurs when deciding to seek care for an obstetric complication. This may occur for several reasons, including late recognition of the fact that there is a problem, fear of the hospital or of the cost that will be incurred there; or the lack of an available decision maker.

- **The second delay** occurs after the decision to seek care has been made. This is a delay in actually reaching the care facility and is usually caused by difficulty in accessing transportation. Many villages have very limited transportation options and poor roads. Some communities have developed innovative ways to address this problem, including prepayment schemes, community transportation funds and the strengthening of links between community practitioners and the formal health system.

- **The third delay** is the delay in obtaining care at the facility. This is one of the most tragic issues in maternal mortality. Often, women will wait for many hours at the referral centre because of insufficient staffing, prepayment policies, or difficulties in obtaining blood supplies, equipment or an operating theatre. The third delay is the area that most planners feel is the easiest to correct. Once a woman has actually reached an EmOC facility, many economic and sociocultural barriers have already been overcome.

Focusing on improving services in the existing centres is a major component in promoting access to EmOC. Programmes designed to address the first two delays are of no use, if the facilities themselves are inadequate.[3] Delays 1 and 3 accounted for the majority of maternal mortality in Ile-Ife.[23, 24]

THE WAY FORWARD

Most of Europe and North America once had levels of maternal mortality comparable to those in the developing world. Near universal access to skilled attendance at birth and to emergency obstetric care has reduced maternal mortality rates to almost zero.

Since 15% of pregnancies will require emergency medical intervention, no matter how carefully they are screened, emergency obstetric care is absolutely essential to reducing maternal mortality and disability.

Developing countries where a reduction in maternal mortality has been successful, share several common programming ingredients. In most of these countries, there has been a gradual shift to professional attendance at birth and a move towards facility-based deliveries. In Cuba, Malaysia and Sri Lanka, where maternal mortality rates are comparatively low, government made a commitment to strengthen the entire healthcare delivery system.[25] This has resulted in a high proportion of births attended by skilled professionals and a reliable referral system for complicated deliveries. In most of these countries, health services are free or at very low cost. Women in Sri Lanka are also likely to use family planning services to prevent 'too-early' and 'too-closely' spaced pregnancies. In Malaysia, a decline in the maternal mortality rate was associated with the introduction of confidential maternal death audits to identify preventable

causes of maternal deaths. These countries have proven that it is possible to reduce maternal mortality in nearly every country. Even in countries where most women deliver at home, or where education and health systems are collapsing under the stress of poverty and AIDS, reducing maternal mortality is possible through a focus on treating complicated deliveries.

Reducing maternal mortality in Nigeria is an achievable objective through the provision of widespread antenatal care, the provision of skilled attendants for all deliveries, adequate management of obstetric emergencies through essential obstetric care and prevention of unwanted pregnancies through family planning.

Role of Antenatal Care

Antenatal visits present an opportunity to address the psychosocial and medical needs of pregnant women, while acknowledging the context in which they live. These periodic health exams allow women to make contact with the healthcare system. Health promotion messages can be individualized during this time and women can be screened for potential risk factors.

Antenatal visits can provide essential services for all pregnant women, such as tetanus toxoid immunization, nutrition education and the distribution of iron and folic acid tablets. WHO recommends a minimum of four antenatal visits. However, it is the quality of the visits rather than the number of visits that is of primary concern. Antenatal care is also an opportunity to offer voluntary counselling and testing for syphilis and HIV, without a separate clinic visit. Pregnant women known to be seropositive can be started on a regimen of drugs designed to minimize vertical transmission. Antenatal visits also offer an opportunity to identify HIV-negative women and provide them with the knowledge to remain negative.[3] Antenatal care also offer intermittent preventive treatment for malaria. This is important, as malaria contributes to anaemia, a significant factor in maternal morbidity and mortality. The treatment usually consists of a single dose chemoprophylaxis, given to pregnant women at least once after quickening. This is combined with the provision of insecticide-treated bed nets.

The Nigeria Demographic and Health Survey 1998 - 2003, showed that among women who delivered, 60% received antenatal care (ANC) at least once. Nigerian women are more likely to receive ANC if they have secondary/higher education and if they are economically empowered. Urban women are 3 times as likely to receive ANC as rural women (46% v 15%). About half of the teenage mothers did not receive ANC; only 58% received iron supplement, 39% received malaria drugs, 40% received two or more doses of tetanus toxoid.[4]

Role of Traditional Birth Attendants

Traditional birth attendants (TBAs), whether trained or untrained, do not have the skills to deal with life-threatening problems. Efforts have therefore shifted from training of TBAs to training of midwives.

The role of the TBA is to facilitate culturally-sensitive liaisons between the health care system and the community. Medical procedures and the administration of medication should be performed by skilled health professionals. In contrast, many midwives and physicians have no training in belief systems, cultural nuances and community organizing. This is where the TBAs can be most effective. They can encourage women to use family planning and antenatal services and can emphasize the need for women to get EmOC at hospitals or other facilities, should complications arise.[3]

Maternity Waiting Homes

Maternity waiting homes are residential facilities where women defined as 'high risk' can await their delivery and be transferred to a nearby medical service shortly before delivery or as soon as complications arise. The goal is to minimize the delay in receiving care for an obstetric emergency by dramatically reducing the transit time. Since the majority of complications occur in women with no apparent risk factors, it is difficult to determine who will benefit from this facility. This is because many medically-classified low-risk women develop potentially fatal complications in labour. In addition, the four-week stay recommended can be a barrier for many women who cannot stay away from their homes for such a long period of time. Although it may allow some to get the needed rest after delivery. Some countries have now progressed from using medical definitions of 'high-risk pregnancy' toward a broader concept based on a combination of distance and socioeconomic and medical risk factors.[3]

Transportation and Formalised Referral Links

Transport difficulties may pose a problem to women who develop complications at night. This can be minimized if emergency transportation options are organized by the community through links with the nearest emergency obstetric unit.

Having formalized referral links between low-level health facilities and the bigger centres will also reduce the rate of late referrals and hence reduce maternal deaths.[12]

Human Rights-based Approach

Since almost all maternal mortality is avoidable, the human 'right to life' principle should be used to promote free access to ante natal care for all pregnant women and skilled birth attendants during childbirth. Moreover, the human rights principles, applied in a culturally-sensitive manner, can be integrated into programmes at the clinical, facility management, and monitoring levels. For example, ways to encourage respectful treatment of patients at the facilities can be implemented. Mechanisms to elicit community perceptions and participation can be applied. At the policy level, human rights principles can inform dialogue and policymaking for health sector reforms.[3,26]

Family Planning

Meeting the existing demand for family planning services, would reduce pregnancies in developing countries by 20% and maternal deaths and injuries by that much or more. While access to family planning will do little to reduce the maternal mortality ratio, it goes a long way in reducing the overall number of deaths related to pregnancy and unsafe abortion.[3]

Skilled Attendants at Birth

Skilled attendants refers to professionally-trained health workers with the skills necessary to manage a normal delivery and diagnose or refer obstetric complications. This usually refers to a doctor, midwife or nurse. They must be able to manage a normal labour and delivery, recognise complications early and perform any essential intervention, start treatment and supervise the referral of mother and baby to the next level of care if necessary.[3] Most obstetric complications occur at the time of labour and delivery. It takes a professional to swiftly recognize life-threatening complications and intervene in time to save the mother's life. As noted before, previous efforts to promote skilled attendance at birth centred on the promotion of traditional birth attendants. A paradigm shift has taken place over the past decade to focus interventions on promoting an increase in professional attendance at delivery.[3] Skilled attendance at birth has been one of the most obvious common programming techniques in countries that have been successful in reducing maternal mortality. Improved access to trained midwives who are supported by the broader health-care system is critical. Adequate support to midwives includes regular and reliable access to medication and supplies, and the respect and authority to make referrals to a higher level of care. In spite of the overwhelming evidence that the use of doctors, midwives and nurses in deliveries is a crucial factor in reducing maternal mortality, only 36% of all deliveries took place in the presence of a skilled attendant in the Nigerian demographic survey.[4] There are many reasons for this. There is a shortage of well-trained and skilled attendants. Another factor is the poor geographic distribution of attendants, with most professionals preferring to remain in the urban areas. Provision of incentives like housing and distance learning programmes to midwives and doctors working in rural and semi-rural areas, and promoting rotation systems with a mix of public and private practice may help retain these professionals. The negative attitudes of some health care providers, as well as administrative bottlenecks, serve as deterrents to the use of health facilities with skilled professionals.[29]

Investing in Human Resources

For almost all developing countries, including Nigeria, human resource strategies are pivotal in improving skilled birth attendance. Poor conditions of service have led to the migration of many nurses, midwives and doctors to foreign countries in search of the 'Golden Fleece'. Skilled midwives are central to efforts to improve pregnancy outcomes. Almost all developing countries that have significantly reduced maternal mortality have emphasized the role of the skilled midwife. In Nigeria, there is the need to have more schools of midwifery to train more midwives. In addition, strategies must ensure that all birth attendants receive the training and orientation they need to provide youth-friendly services. Limited access to reproductive health services leaves adolescents particularly vulnerable to unintended pregnancy. Sound human resource and management strategies should also ensure that pay scales, working conditions and career advancement opportunities are sufficient to maintain the equitable distribution of workers across regions, boost morale and reduce the number lost to brain drain. Mechanisms to maintain and upgrade providers' clinical skills and abilities are needed.[27]

Upgrading Health Institutions

Upgrading health institutions is a critical strategy for improving delivery care. As medical facilities and referral systems begin to offer a higher quality of care, communities will take note of and build demand for services. Many women in Nigeria do not utilize health

facilities because of the perceived inefficiency in the system as well as the administrative bottlenecks, negative attitude of staff and exorbitant user fees. In addition to addressing the human resource issues noted above, institutional improvements may include physical renovation, more support staff, implementation of standards of practice, improved management and supervision, and the purchase, distribution and maintenance of equipment. Attention should also be given to building rapport between women and health providers.

Cultural sensitivity must be integrated into all operational levels (clinical, managerial, monitoring and evaluation) to ensure that all women are treated with dignity and respect. This is particularly relevant for facilities that serve indigenous populations. Health professionals may require sensitization to the cultural norms surrounding delivery.[27]

Role of Men and Other Influential Members of the Community

Men are key decision-makers in maternal and newborn care-seeking behaviour. Men also decide if and when a woman uses contraception. They need to understand the needs, risks and danger signs of pregnancy, childbirth and postpartum periods. They decide how and when to make resources available for their wife's care. Promotion of the role of men as partners and fathers is essential for their involvement and support.[28] This is very important in some parts of Nigeria, where a woman cannot seek care for pregnancy complications, except with the express permission of the husband.

Religious leaders also wield a lot of authority over their followers, hence there is the need to seek their support and involvement in the process of reducing maternal mortality through workshops and seminars.

Community leaders, family members, TBAs and other influential people can be positive agents in support of women and neonate health needs. Older family members, such as the mother-in-law, have strong, culturally-sanctioned powers for decision-making and care in issues like the diet of the pregnant woman, workload and household responsibilities and the use of emergency services. Health education and coordination with the education sector will be useful to ensure the inclusion of content in primary and adult education.[28]

Community Financing and Transport Schemes

The availability of financial and transport schemes can affect individual and household decision-making processes, facilitate access and therefore, reduce associated delays in receiving skilled care. In Nigeria, transport difficulties and the cost of health care are two major inhibitions when making a decision to use health care facilities. The National Health Insurance Scheme (NHIS) is yet to be extended to the trader and the peasant farmer, who are mainly illiterates and therefore at a higher risk of maternal deaths. There is the need to make obstetric services free for all women in Nigeria. This will increase the utilization of formal health services by most poor women. There is also the need to provide emergency transportation services for women with pregnancy complications. This can be coordinated by the local area government council in consultation with the community leaders. In the long run, however, there is the need to create insurance programmes for obstetric emergencies through women's cooperative societies and women's religious groups.

CONCLUSION

Maternal mortality reduction depends on a facility-based health system that works. The death of a woman in childbirth is the ultimate failure of the health system. An average of seven women die each hour of the day in Nigeria from complications during pregnancy and delivery. The problems associated with pregnant women usually predate the pregnancy. It may start from infancy with poor nutrition.[30] Hence, efforts at reducing maternal mortality in the long run must address all the disadvantages of Nigerian women from childhood.

The millennium development goals underscore the importance of skilled care during birth as a means of reducing maternal mortality and morbidity. Providing skilled attendants without ensuring the overall functioning of the health system would not achieve the goal of reducing maternal mortality.[27] Skilled attendance during childbirth demands a continuum of care, requiring a range of skills and capacities. We know what works and what does not work.[31] What is needed is the political will to mobilize the needed resources to tackle this evil.

Sometimes, traditional practices, cultural or religious beliefs present barriers to obstetric care that require great sensitivity and patience to overcome.[32,33]

The question asked by William Farr in 1838 in England and quoted by Maine and Rosenfield is apt for Nigeria today, 'A deep, dark continuous stream of mortality . . . how long is this sacrifice to go on'? Maine and Rosenfield added that, 'the lack of progress is not due primarily to scarcity of resources'. A great deal can be accomplished

by making better use of existing resources.[34] It all depends on what we feel the life of a Nigerian mother is worth.

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The potential of lipids to nutrition and biomedical research – a review

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SUMMARY

Lipids are found in all animal cell membranes and have been suggested to play important roles in a wide variety of cellular functions, including cell-cell interactions, cell growth and differentiation, transformation and signal transduction. Heart disease has been found to be favourably affected by the consumption of certain unsaturated fatty acids. Unsaturated fatty acids lower plasma total cholesterol and 'bad' cholesterol levels when substituted for saturated fatty acids. However, trans-monounsaturated fatty acids were found to be intermediate between cis-monounsaturated fatty acids and long-chain saturated fatty acids in their effects on plasma total and 'bad' cholesterol concentrations. Cholesterol levels are related to cardiovascular disease. Synthetic lipids have been used for bilayer stabilization, temperature/pH-sensitive liposomal drug delivery, tumor imaging and two-dimensional crystallization on lipid bilayers.

INTRODUCTION

Lipids are fatty acids and their derivatives, and substances related biosynthetically or functionally to these compounds. Lipids are important dietary constituents because of their high energy value, fat-soluble vitamins and the essential fatty acids which are found in the fats of natural foods.

Lipids consist of fatty acids esterified with an alkanol to which other compounds may also be bound. Depending on the nature of the alkanol and the attached compounds, lipids are classified into phospholipids and neutral lipids. The neutral lipids (triglycerides) constitute the main part. Phospholipids serve structural and metabolic purposes in the body while triglycerides serve mainly as storage of energy as fat. Consequently, the content of triglyceride may fluctuate depending on the energy status, while the content of phospholipids remains fairly constant.

This paper aims at exposing some novel areas of lipids to nutrition and clinical applications.

TYPES OF LIPIDS

Phospholipids: The backbone of phospholipids is the glycerol molecule, which also forms the backbone of triglycerides. Phospholipids consist of two fatty acids (diglyceride), a phosphate group and an alkanol. Phospholipids and cholesterol are the principal components of nearly all cell membranes, although different cells have varied quantities of phospholipids in their membranes. The alkanol portion of phospholipids protrudes away from the membrane, whereas the two fatty acids jut into the membrane. The middle fatty acid (in the second position) is usually unsaturated, whereas the end fatty acid (in the first position) is usually saturated. Examples of phospholipids include: lecithin, cephalin, sphingomyelin, phosphatidyl inosital, cardiolipins and lysolecithins.

Sphingolipids are lipids containing the long-chain amino alcohol (sphingosine) or its derivatives. They are found in high concentrations in the brain and other tissues of the nervous system. Examples include: D-erythro-sphingosine, sphingomyelin, ceramides, cerebrosides, brain sulfatides, ganglioside–porcine brain.

The sphingosine derivatives (soybean) include: glucosylceramide; while phytosphingosine and its derivatives (yeast) include: D-ribo-phytosphingosine-1-phosphate, N-acyl phytosphingosine C2, N-acyl phytosphingosine

C8, N-acyl phytosphingosine C18. The phospholipids occurring in fish are mainly lecithin and cephalin, which account for about 60% and 20% of the total phospholipids, respectively.[1] In most marine fishes, phospholipids have been found to be higher in their content of the PUFA C20:5 and C22.6, than the triglycerides from the same fish.

The phospholipid or phosphatide content in commercial fish oils act as emulsifying agents and catalyst poison in the hydrogenation of fish oils. The quantity of phospholipids present in oil is usually measured in terms of parts per million or microgrammes per gramme (µg/g) of phosphorus found in the oil. The phosphorus content of fish oils is largely dependent on the efficiency of cleaning of the extracted oils

Phosphatidyl choline finds applications as phosphalipase inhibitors, platelet-activating factors, central nervous system agents, cardiac agents and anti-tumour agents. This is due to the absence of reactive functional groups that would require protection in synthesis.

Neutral lipids: They constitute the main part of fish oils and may fluctuate depending on the energy status. They contains less polyethene fatty acids, but more of the monoethylenic fatty acids. They mainly serve as storage of energy as fat. Because they are uncharged glycerides, cholesterol and cholesterol esters are termed neutral lipids.

Derived lipids: These include substances derived from the above groups by hydrolysis of fatty acids (both saturated and unsaturated), glycerol, steroids, alkanols in addition to glycerol and sterols, fatty alkanals and alkanones.

Biologically relevant synthetic glycerol-based lipids include: phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylserine (PS), phosphatidylinositol (PI & PiP's), phosphatidic acid (PA), phosphatidylglycerol (PG), cardiolipids (CL), diacylglycerides (DG), cholesterol (plant-derived) head group modified derivatives, PEG lipids, functionalised lipids for conjugation, phospholipids with multifarious head groups, polyphenolic lipids for pH-sensitive liposomes, metal-chelating lipids, antigenic phospholipids, doxyl - lipids.

Fatty acid-modified derivatives include: lyso phospholipids (monoacyl), alkyl phosphocholine, oxidized lipids, biotinylated, ether lipids, plasmologen lipids, diphytanoyl phospholipids (black lipid membranes), polymerizable lipids, brominated phospholipids, fluorinated phospholipids, doxyl lipids, fluorescent lipids.

Ether lipids include: diether lipids (diakyl phosphatidylcholine), diphytanyl ether lipids (alkyl phosphocholine, dodedylphosphocholine), O-alkyl diacylphosphatidylcholinium (1,2-diacyl-sn-glycero-3-ethylphosphocholine), synthetic PAF & derivatives (1-alkyl-2-acyl-gycero-3-phosphocholine & derivatives).

Glycerol-based lipids are: choline (phosphatidylcholine and platelet activation factor (PAF)); ethanolamine (phosphatidylethanolamine); glycerol (phosphatidyl-DL-glycerol); Inositol (phosphatidylinositol pi(4)p, pi(4,5) p2), serine (phosphatidylserine), cardiolipin (sodium salt), phosphatidic acid, egg derived, lyso (mono acyl) derivatives (lysophosphatides), hydrogenated phospholipids, lipid tissue extracts (brain & egg *E. coli* & heart, liver & soy).

Bioactive lipids are platelet activation factor lipids, diacylglycerol pyrophosphate (DGPP), P1 & PIP's inositol phosphates, inhibitors of mitochondrial ceramidase, cationic ceramides.

PROPERTIES OF LIPIDS

Lipids are found in all animal cell membranes and have been suggested to play important roles in a wide variety of cellular functions, including cell-cell interactions, cell growth and differentiation, transformation and signal transduction. To better understand the various roles lipids play in these complex processes, it is necessary to elucidate the mechanisms responsible for generating and maintaining the intracellular distribution of lipids in cell membranes.

In lipids, the presence of particular groupings is associated with activities of varying kinds, but it is not a guarantee of biological activity. However, individual chemical groupings can be significant in two ways. They may be essential for the manifestation of a particular type of chemical reactivity or stereochemical arrangement. They may not be replaced by alternate groupings without a loss of their characteristic function, unless the alternative groupings produce a molecule in which the chemical and physical properties are very close to those of the prototype. Secondly, individual groups may exert characteristic effects in modifying the intensity of a type of biological activity which is exhibited in compounds having a common molecular basis.

When a particular grouping is responsible, through its chemical reactivity, for producing biological activity, it is important to bear in mind the quantitative aspect of its chemical reactivity. If the grouping is very reactive, the substance may react easily with a variety of cell constituents, perhaps even with water and in consequence, it may not be able to reach a site within the organism where a specific cell constituent can be affected. At the other extreme, if the chemical reactivity is too low, biological activity will be diminished, perhaps to the point of disappearance.

Alkyl groups may have a determining effect on the physical properties of an organic substance. The longer the chain or in the case of branched chains, the higher the molecular weight, the greater the effect. In cases where biological activity is largely influenced by the physical properties of the substance, such as its solubility, diffusibility or surface activity, the nature of the alkyl group will largely influence the biological activity. The methyl group is unique among the alkyl groups because it plays a special part in metabolism. It can also affect biological activity by the replacement of active hydrogen atoms, thus distorting the general chemical reactivity of the molecule, either by blocking chemically reactive positions or by activating other positions.

The function of hydroxyl groups in biologically active compounds may depend on whether the OH group confers or modulates activity by virtue of its effect on physical properties or whether it undergoes a significant chemical reaction. The substitution of OH for H affects biological activity profoundly. Polyhydroxyl compounds are characterized by their capacity to enter into a union with other molecules and with themselves by H-bonding. Such unions can, by the stereochemical orientation of the OH groups, determine such properties as specific enzyme affinities. Also OH group reactions are based on their capacity to accept activated groups through the action of group-transferring enzymes.

Thiol groups occur widely in natural products, and the biological activity of these, are in many instances, quite clearly associated with their characteristic chemical reactivity. Thiol groups as components of apoenzymes, are vital to the function of many enzymes. In these more complex molecules, only a proportion of the thiol groups may be available for chemical reaction. Other thiol groups may be relatively inaccessible, either because they are screened by the macromolecular structure or possibly because they are only revealed after breaking of labile intramolecular bonds. Thiol groups obscured in this way are also found in compounds of lower molecular weights. The interconversion of thiols and disulphides by oxidation- reduction reactions, provides a possible method whereby biological activity can be exhibited, as such systems might well regulate or interfere with normal metabolic oxidation-reduction systems. Thiols also have the capacity to add to double bonds, particularly those in aß-unsaturated ketonic compounds. Thiols can as well form insoluble mercaptides with heavy metals.

The ether linkage provides a valency angle approximately the same as a carbon-carbon link. It is therefore possible for an oxygen (or sulphur) atom to be interposed in an alkyl chain without major stereochemical alteration.

The physicochemical properties of molecules are fundamentally changed by the introduction of the COOH group. These changes may result in the creation of conditions necessary for biological activity or for altering the nature of the biological effect, or they may have the reverse effect, the destruction of any activity which was originally present.

Unsaturation in compounds may influence its stereochemical considerations, especially where the possibility exists in the unsaturated compound of *cis-trans* isomerism. One of the isomers of the unsaturated form may have some characteristic activity which is either not shown by the saturated substance or is only shown to a diminished degree. Unsaturation in compounds may also affect their physical properties. Chemically, an isolated double bond does not appear to possess a sufficient degree of reactivity to enter into ready unions with cell constituents, for if it were otherwise, the unsaturated hydrocarbon might be expected to exhibit a greater variety of reactions than they actually do. However, when the double bond is chemically activated by a neighbouring group, a different state of affairs prevails.

ECONOMIC IMPORTANCE OF LIPIDS TO NUTRITION AND MEDICAL RESEARCH

With the focus on concepts such as glycaemic index, macronutrient ratios and food groups, essential fatty acids (EFA) are one of the most neglected aspects of nutrition in modern society. Omega-3 FA is of particular importance, its deficiency in the diet, particularly EPA and DHA, may play a strong role in many of the widespread and interrelated conditions of today, such as

cardiovascular disease, inflammatory conditions and obesity. Although they are most commonly emphasized only when one of these conditions is present, ensuring an adequate intake can play an important preventive role.

POLYUNSATURATED FATTY ACIDS (PUFAs)

These are long-chain FAs (C14 - C24) (LCFA). They are absorbed and metabolized more slowly than either medium-chain fatty acids (MCFA) (C6 - C12) or short-chain fatty acids (SCFA) (C2 - C6). Much of the LCFAs may be lost as calcium FA soap in the faeces.[2]

Fatty acids that cannot be synthesized by the body from other FAs, and therefore must be obtained from food, are called essential fatty acids (EFAs). The human body lacks the desaturase enzymes required for their production. EFAs are classified into two families: omega-3 (ω -3) and omega-6 (ω-6). Omega-3 FAs are synthesized from α-linoleic acid (ALA) and they include: 9,12,15 - octadecatrienoic acid; 6,9,12,15 - octadecatetranoic acid, 8,11,14,17-eicosatetraenoic acid, 5,8,11,14,17-eicosapentaenoic acid, 4,7,10,13,16,19 - docosahexaenoic acid (DHA).

Omega-6 FAs which are synthesized from linoleic acid, include: 9,12-octadecatrienoic acid, 6,9,12-octadecatrienoic acid, 8,11,14 - eicosatetranoic acid, 5,8,11,14-eicosatetranoic acid.

These two families are the result of increasing chain lengths and double bond formations. They compete for the same enzymes for double bond formation (desaturase enzymes) and those for lengthening the carbon chain (elongase enzymes). Elongase enzymes add the carbon atoms in pairs to the delta end (δ) of the fatty acid chain. *Tilapia* sp. possess enzymes that desaturate and elongate fatty acids of the ω-3 and ω-6 series to provide sufficient levels of the long chain PUFA necessary for membrane function and fluidity.[3,4]

Polyunsaturated fats have often been recommended to reduce coronary heart disease.[5] But, all saturated fats do not have the same effect on cholesterol synthesis in the liver, only those with chain lengths of 12, 14 and 16 (dodecanoic, tetradecanoic and hexadecanoic acids) have been shown to elevate blood cholesterol. Tetradecanoic acid (found in high concentrations in coconut and palm oil) elevates cholesterol the most,[6] while octadecanoic acid (18-carbon, saturated) has been shown to lower cholesterol by 21%, even more than 9-octadecanoic acid (18-carbon, mono-unsaturated) which lowers LDL by 15%.[7]

Eggs from hens contain excellent, low cost, high quality protein, and a balanced distribution of minerals and vitamins.[8,9] Eggs, however, have a relatively high cholesterol content and attempts at reducing the cholesterol content have not been successful.[10,11] However, the fatty acid composition and contents of fat-soluble vitamins and certain trace minerals can be altered by diet.[12,13] Efforts by the poultry industry to market health-valued products, have focused on increasing the very long-chain PUFA content of meat and eggs. However, increasing the amount of PUFAs in the diet increases the degree of unsaturation, which may in turn increase the susceptibility to lipid oxidation.

Also identified was the potential human health risks associated with increased consumption of ω-3 PUFAs due to increased consumption of lipid oxidation products. Problems could also arise from increased *in vivo* production of lipid oxidation products and the depletion of tissue levels of vitamin E.[14,15] It was observed that egg yolk lipids from free range native hens are inherently resistant to oxidative determination, since the typical egg yolk contains only 1.4% very long chain PUFAs,[16] but could rise to about 5% on the feeding of PUFAs to animals.[17]

The EPA and DHA found in fish increases the plasma concentration of PUFAs more than fish oil supplements. Fish oil supplements therefore are a more convenient and less expensive source of EPA.

Fish oil triglycerides have been offered in liquid, capsule, tablet and powder forms, as natural products, reflecting the composition of the fish species processed.

Researchers[18,18,20] have cited evidence that the oils (lipids) in fish, rich in long-chain ω-3 FA, may help reduce the incidence of the following diseases in humans: aggression and depression, neurological dysfunction, including visual symptoms, among others.

CONJUGATED LINOLEIC ACID

Conjugated linoleic acid (CLA) is a naturally occurring fatty acid with a conjugated double bond. It has a number of documented beneficial properties for humans and animals. The hydrogenation of vegetable oils with a high quantity of CLA might provide the possibility for their utilization as health-promoting food ingredients. However, some are of the opinion that commercial sources of food grade quantities of this unusual non-methylene interrupted FA will be required before the therapeutic benefits are realized in humans.[21]

TRANS FATTY ACIDS (TFAs)

TFAs are unsaturated fatty acids with at least one double bond in the trans configuration. The smaller double bond angle and a linear acyl chain results in a more rigid and straight molecule with a high melting point that approaches a corresponding saturated fatty acid. The structural similarity with saturated fatty acids, lack of specific metabolic functions of their parent polyunsaturated fatty acids (PUFA) and its competition with essential fatty acids (EFA) in many complex metabolic pathways, increases low density lipoprotein (LDL) to a degree similar to that of saturated fats, but reduces high density lipoprotein (HDL) cholesterol.[22] HDL picks up excess fats and carries them to the liver, while LDL drops fats on blood vessel walls rather than carry them to the cells where they are needed. TFAs exhibit competitive interactions with the EFAs by inhibiting its incorporation into membrane phospholipids and by reducing the conversion of EFA to eicosanoids in different cells.[23] Therefore, TFA ingestion results in EFA deficiency. However, the incorporation of TFA into membrane phospholipids may influence the physical properties of the membrane, as well as the activities of the membrane-associated enzymes.[24]

Breast-fed infants have a greater intake of TFA through their mother's milk (2-5% of total milk FA) which reflects the maternal consumption of these fatty acids.[25]

Cardiovascular Disease

Fish oil prevents coronary heart disease (restenosis, cardiac arrhythmias), mild hypertension (high blood pressure) because of its anti-arrhythmic properties, improved endothelial function, anti-inflammatory properties and reduction in serum triglycerides, with both EPA and DHA playing important roles.[26]

Although, PUFAs have often been recommended to reduce coronary heart disease, not all saturated fatty acids have the same effect on cholesterol synthesis in the liver. Only the saturated fatty acids of chain-length 12, 14 and 16 have been shown to elevate blood cholesterol, thus depressing the immune system and increasing the incidence of cancer; C14 elevates cholesterol the most.[6] Octadecanoic acid (C18:0) has been shown to lower cholesterol by 21%, even more than 9-octadecanoic acid (C18:1), which lowers low density lipoprotein (LDL) by 15%.[7,27] Sano M et. al. asserted that TFA are more atherogenic than saturated fatty acids (SFA) because they increase lipoprotein (a), a non-dietary-related risk of atherogenesis, to levels higher than the corresponding chain-length SFA.[28] TFA also decreases HDL in animal species such as pigs[28] and rats.[29,30]

Experts in the field of circulation in the United States noted that eating oily fish at least twice a week might help prevent sudden death from a heart attack, as FAs in the fish reduces the incidence of dangerous irregular heart rhythm. Studies of individual heart cells showed that the fatty acid blocked excessive Na and Ca currents in the heart, which could otherwise have caused dangerous, unpredictable changes in its rhythm.[31]

Phosphatidylethanolamine derivative lipid analogs have been found to possess powerful antihypertensive properties. Also, it is reported to cause platelets to change shape, aggregate and release their granule contents at concentrations between 10^{-11} and 10^{-10}M.

Fish Oil and Brain Development

DHA plays a very important role in brain development and the maintenance of normal brain function in adults.[32] Impaired development of brain and visual acuity, reduced intellectual capacity in infants can also be prevented by this fatty acid. DHA increases the IQ of children at age four by an average of 4.1 points.[33] DHA is preferentially taken up by the brain, where it then enhances membrane fluidity, which in turn changes the signaling properties of neurons and affects the function of the blood-brain barrier.[34]

Anti-inflammatory Properties

Fish oil has been explored in a number of inflammatory and autoimmune conditions. These include: rheumatoid arthritis, Crohn's disease, ulcerative colitis, psoriasis, lupus erythematosus, multiple sclerosis, migraine, asthma and cystic fibrosis; and it usually has a significant beneficial effect.[35,36] Mechanisms of action include: the displacement of 6,8,10,12-eicosatetraenoic acid (which is pro-inflammatory), suppression of pro-inflammatory cytokines and changes in adhesion molecule expression.[35]

Researchers at the Harvard Medical School and Brigham Women's Hospital in the United States in 2005, found that a diet rich in fish oils raised the body's production of an anti-inflammatory fat, thus, possibly reducing the effects of arthritis. This diet however, worked best according to their report, when combined with low aspirin doses. Another study by Edinburgh and Stirling Universities in connection with Edinburgh Royal

Hospital for Sick Children, suggested that fish oils could help deal with the effects of childhood autism.

The 6,9,12-octadecotrienoic acid has been shown to be effective against inflammation from rheumatoid arthritis in a number of studies. It may be that rheumatoid arthritis patients suffer from impaired function of desaturase enzymes, preventing 5,8,11,14-eicosatetranoic acid formation. In ulcerative colitis, an inflammatory condition in which desaturase enzymes are normal, both ω-3 oils from fish and perilla have been used for treatment.[37]

Conjugated linoleic acid (CLA)prevents or cures cancer,[38,39,40] atherosclerosis[41], and type-2 diabetes,[42] because of its unique chemo-protective and antioxidant properties. CLA may regulate cytokine production to strengthen muscle and bone activity in humans.[43] The fat partitioning activity of CLA reduces fat synthesis in mice and abdominal circumference in humans.[44,45]

L- PHOSPHATIDYLCHOLINE (tissue-derived)

Natural phospholipids are readily oxidized, because in addition to saturated hydrocarbons, they contain multiple unsaturated hydrocarbons. The linkage between the glycerol and the long-chain hydrocarbon is predominantly the ester bond. In the sn-2 position, the ester bond, is the only type of linkage. However, in the sn-1 position of phosphatidylcholine from the liver, heart and brain, several linkages exist: ester-linked hydrocarbons and vinyl ether-linked hydrocarbons (plasmalogen).

It was observed that oxidized 1-palmitoyl-2-arachidonyl -sn-glycero-3-phosphorylcholine(OxPAPC), a component of minimally modified low density lipoprotein (MM-LDL), activates the endothelial cells to bind monocytes.[46] The 1-palmitoyl-2-(5-oxovaleroyl)-sn-glycero-3-phosphorylcholine (POVPC) and 1-palmitoyl-2-glutaroyl-sn-glycero-3-phosphorylcholine (PGPC) are potent regulators of monocyte-specific endothelial interactions and they play a dominant role in a number of chronic inflammatory processes where oxidized phospholipids are known to be present. Structurally, similarly oxidized phospholipids differentially regulate endothelial binding of monocytes and neutrophils.

Biological diversity of detoxified lipid A is exemplified by its multi functional activities, including acting as an adjuvant,[47] tolerance to *Salmonella enteritidis* LPS and tumor necrosis factor alpha (TNF-alpha),[48] attenuating platelet thrombosis[49] and attenuating interoperative ventricular dysfunction 'stunning' associated with aortic cross-clamping and reperfusion.[50]

VACCINES

Vaccine development is dependent on immunological adjuvants that mediate and promote a wide variety of immune responses. The immunological response to detoxified lipid A is dependent on the vehicle formulation. An aqueous vehicle or an oil-in water emulsion can be used to modulate the vaccine strategies being investigated today.[47] Nakatani et. al. suggested that detoxified lipid A may induce an antigen-specific primary immune response by provoking the migration and maturation of dendritic cells, which are the physiological adjuvants of the immune system.[51]

Phosphatidyl choline finds application as a phosphalipase inhibitor, platelet-activating factors, central nervous system agents, cardiac agents and anti-tumour agents. This is due to the absence of reactive functional groups that would require protection in synthesis.

BODY COMPOSITION

Fish oils promote the activation of peroxisome proliferators-activated receptor alpha (PPARalpha) and peroxisome proliferators-activated receptor gamma (PPARgamma), which in turn increases the production of various enzymes that break down fat.[52,53,54] It also deactivates a number of lipogenic (fat-forming) enzymes.[53,54,55]

The human body can manufacture most of the fats it needs, including cholesterol, saturated and unsaturated fatty acids. The body cannot make ω-3 or ω-6 fatty acids, because human metabolism cannot add a double bond to a fatty acid that is more than 9 carbons away from the carboxylic end. For the same reason, the body cannot convert ω-3 to a ω-6 fatty acid or vice versa. But, the body can make ω-9 and ω-3 and ω-6 fatty acids from 9, 12, 15-octadecotrienote and 9,12-octadecadienoic acid, respectively. It can also add more double bonds closer to the carboxylic end of ω-3 and ω-6 FAs. These fatty acids compete for the same enzymes for forming double bonds (desaturase enzymes) and lengthening the carbon chain (elongase enzymes). Elongase enzymes add oxygen atoms (in pairs) to the carboxylic end of the fatty acid chain. Insulin resistance in adult-onset diabetes is associated with fewer membrane long-chain unsaturated

fatty acids, due to impaired desaturase and elongase enzyme function.[56]

Feeding laboratory animals diets rich in ω-3 fatty acids (linseed or fish oil) reduces natural killer cell and cytotoxic T-lymphocyte activity,[57] and stimulates the more antigen-specific immunoglobulins IgM and IgG.[58] One experiment showed that both fish oil and safflower oil reduced the secretion of interleukin-6 (a cytoxine that activates lymphocyte immune-cells and increases antibody production), but that only fish oil inhibited the secretion of tumor necrosis factor alpha (a cytokine that increases fever, shock and blood vessel permeability).[59]

Polyunsaturated 'cis' fatty acids can be beneficial in cell membranes by preventing the tight packing of fatty acids in membranes, thereby making the membranes more 'fluid'. Membrane fluidity is important for the optimal functionimg of most cells in the body. But, membrane fluidity is especially important on portions of cells that act as receptors for hormones or neurotransmitters. The typical North American eats three times as much saturated fat as unsaturated fat, yet animal experiments show that insulin receptor responsiveness is substantially improved when dietary unsaturated fat is greater than saturated fat.[60] With aging, however, cell membrane fluidity declines in part because of the increasing amount of cholesterol in the membranes, but more importantly because of free-radical oxidation.[61] Antioxidants that protect cell membranes, like vitamin E, are extremely valuable in opposing membrane oxidation.

To minimize lipid peroxidation, essential fatty acid supplements should be taken with about 500mg of vitamin E per day. But, for smokers, vitamin E may not be adequate to reduce oxidation of fish oil in LDL-cholesterol. Some medical authorities have cautioned against too much fish oil consumption by smokers.[62]

POSSIBLE DISADVANTAGES OF FISH OIL USE

PUFAs can be a health hazard, because C = C can lead to free radical formation and reactions with oxygen to form unstable lipid peroxide compounds, containing the same unstable oxygen-oxygen bonds found in H_2O_2. Lipid peroxidation and free radicals can cause cancer and may accelerate aging. High rates of lung cancer among women in China have been associated with lipid peroxidized oils in fumes from cooking polyunsaturated vegetable oils in a wok.[63] Hot oil in the open air is subject to much lipid peroxidation. Fast-food restaurants that fry foods in the same oil all day, serve lots of lipid peroxides to their customers.

The use of saturated oil in deep fat frying encourages the formation of heterocyclic amines in the field products. The saturated oil may undergo hydrolysis to form a large amount of free fatty acids (FFA) during heating, which in turn facilitates the degradation rate of lipids and the formation of heterocyclic amines.[64] Frying may as well increase the ratio of PUFA to SFA and that of ω-6 to ω-3, giving rise to a negative effect on the benefits related to intake of EPA and DHA. Therefore, vegetable oils rich in ω-6 PUFAs should be avoided in pan and deep-fat frying, if an increase of ω-3 PUFAs is desired.[65]

It was asserted that longer chain ω-3 PUFAs may not be affected by deep-fat frying, due to the formation of geometrical fatty acid isomers of long-chain PUFAs.[66]

High doses of fish oil may decrease immune function, impair bacterial resistance, increase LDL cholesterol and decrease HDL cholesterol. It also could cause the thinning of blood and therefore may increase the likelihood of bleeding.

Increased amounts of PUFAs in diets increase the degree of unsaturation and may increase susceptibility to lipid oxidation.[67] which has been identified as a potential human health risk associated with increased consumption of ω -3 PUFA due to increased consumption of lipid oxidation products and depletion of tissue levels of vitamin E.[14]

OTHER AREAS OF LIPID APPLICATION IN NUTRITION AND BIOMEDICAL RESEARCH

A wide variety of fatty acids and fatty acid derivatives have found numerous applications in both biochemical and industrial fields. These include:

- Detection of adulterated fats and oils
- Identification of specific triglycerides causing graininess in shortening and margarine
- Identification of specific triglycerides giving some fats and oils unique suitability for confectionaries
- Increased utilization of dietary fats in infant feeding
- Defining mechanisms of intestinal fat absorption
- Defining pathways for triglyceride biosynthesis
- Identification of specific triglycerides which are active substances producing aggregation

- Diagnosis of disease by characterization of distinctive phytanate triglycerides found in plasma which might possibly reflect metabolic disorders.

DEVELOPMENT OF FUNCTIONAL PHOSPHOLIPIDS

This technology seeks to replace fatty acids found in plant phospholipids with essential ω-3 fatty acids. The important effects of functional phospholipids on humans may include: better memory, learning, concentration and a reduction in or a delay in the aging processes in the brain. By improving on traditional ω-3 triglycerides, the incorporation of long-chain ω-3 fatty acids in phospholipids helps the product to increase the elasticity of cell membranes and thus their penetrability when substances are transported into and out of cells. In addition to increased absorption and improved bio-efficiency, the innovation also facilitates stable and predictable product quality. The technology paves the way for unique benefits by enabling the composition of phospholipids to be tailored to produce optimal health-promoting effects suitable for the pharmaceutical, neutraceutical, food ingredients and animal feeds.

MECHANISMS OF ENDOCYTOSIS AND INTRACELLULAR SORTING OF LIPIDS

Glycosphingolipids (GSLs) play important roles in a wide variety of cell functions, including cell-cell interactions, cell growth and differentiation and signal transduction. GSLs can interact with cholesterol to form membrane micro domains. Data from many studies suggest that the plasma membranes (PM), GSL and cholesterol complex may be tightly regulated. To achieve this regulation, cells must balance complex processes underlying the intracellular transport of GSLs with their synthesis and degradation.

- Glycosphingolipiod regulation of Glut4 storage vesicles in 3T3-L1 adipocytes.
- Sphingolipid modulation of cell migration in MCF-7 breast cancer cell lines.
- Lipid recycling between the plasma membrane and intracellular organelles.

ROLE OF VARIOUS RAB PROTEINS AND CHOLESTEROL IN REGULATING LIPID TRANSPORT

Studies have shown that the occurrence of defective lipid transport and sorting along the endosome/lysosome and recycling pathways in a broad collection of sphingolipid storage diseases (SLSD); fibroblasts and over expression of selected Rab GTPases (Rabs 4,7 or 9) corrects defective membrane traffic in several SLSDs and dramatically reduces accumulation of cholesterol, and perhaps other stored lipids. Therefore, it could be that modulation of intracellular vesicular transport should be considered as a new approach for clearing stored lipids from cells in various diseases.

MEMBRANE TRAFFIC IN SPHINGOLIPID STORAGE DISEASES

Sphingolipid storage diseases (SLSD) generally result from a defective lysosomal hydrolase or activator protein, which leads to an accumulation of endogenous lipids in the lysosomes of many different cell types in the body. In addition, cells from patients with Niemann pick type C (NP-C) and mucolipidosis type IV (ML-IV) diseases accumulate lipids in the lysosomes, but this accumulation is not the result of a defect in hydrolysis, but a defect in transport to or from the lysosomes. Correcting lipid storage defects in NP-C disease can be achieved by modulating lipid trafficking.

SPHINGOLIPID MODULATION OF EOSINOPHIL FUNCTION

Lipid traffic and lung deformation surfactant constituents in the lung are synthesized by alveolar epithelial type II (AEC II) cell and secreted into the alveolar lumen. Components of the surfactant are subsequently internalized and selectively transported to the lamellar bodies (LB) of the AEC II cells in a process termed 'recycling'.

ROLE OF SPHINGOLIPIDS IN FUNGAL INFECTIONS AND RELATED INFLAMMATORY RESPONSES

- Lipid transport in oligodendrocytes.
- Membrane traffic in mucolipidosis type IV disease.
- Synthesis of lipid analogs for trafficking studies.

Biotin phosphatidylethanolamine (PE) has been used for bilayer stabilization,[68] temperature/pH-sensitive liposomal drug delivery,[69] tumour impaging,[70] two-dimensional crystallization on lipid bilayers[71,72,73] and immobilization of liposomes on gel beads for chromatographic analysis of drug membrane partitioning.[74] Its use for *in vivo* targetting applications

utilizing liposomes containing monosialoganglioside (GM1) or polyethylene glycol (PEG) lipid derivatives has also been studied.

CONCLUSION

The consumption of lipids has increased steadily in parallel with the increasing commercial production of margarine and shortening. Lipid consumption within a given population will differ greatly depending on lifestyle and socioeconomic status. The estimated average consumption in developed countries masks the wide range of applications that lipids can be put to. Although, the average absolute application of lipids may not have been pursued, studies from overseas suggest that there may be a market potential derivable from intense lipid research. Although, it is difficult to ascertain the absolute levels of lipid research in Nigeria, it is conceivable that investment in lipid research could actually be beneficial to the growth of the Nigerian economy.

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Original Research

Effect of ingestion of ethanol extracts of *Garcinia kola* seed on leucocytes in Wistar rats

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SUMMARY

The objective of this study is to investigate the ingestion of crude ethanol extracts of *Garcinia kola*, i.e., the effect of the active ingredient, biflavonoid, on leucocyte count. Ninety male Wistar rats, with average weight of 200g, were divided into three treatment groups (A, B & C), with 30 rats per group. Groups A, B and C received 20%, 30% and 50% w/w equivalent of the ethanol or water extract prepared diet of feed for two weeks. At the onset of the experiment, 10 animals were sacrificed from each group, to serve as the control group. At the end of the 1st and 2nd week, 10 rats were sacrificed from each group and their leucocyte count and white blood cell differential count were determined. The analysis of the results showed that the leucocyte count values reduced significantly ($P < 0.05$) in all the groups, when compared with their control values, with the exception of sub-group B2, which showed a non-significant decrease. The differential white blood cell count showed variations in the values of the neutrophil, lymphocytes, eosinophil and monocytes in the treatment groups. These variations were not significant ($P < 0.05$), although, they did not fall below the normal physiological range of the experimental animals. The reduction in the leucocyte count may be due to alterations in the rate of production of the various leucocyte pools, which might have been initiated by the biflavonoid content of *G. kola* seed. Therefore, its use, especially for the treatment of potentially immunosuppressive diseases, should be regulated to mitigate excessive immune-suppression and its complications.

INTRODUCTION

Garcinia kola seed, generally known as bitter kola, belongs to a family of tropical plants known as Guttifera.[1] It is widely consumed and used in traditional medicine for various therapeutic purposes, based on supposed pharmacological effects of the active component (flavonoid) in the seed and other parts of the plant.[2] The fact that physiological studies are still lacking to validate the therapeutic efficacy or otherwise of *G. kola*,[3] its use in African traditional medicine cannot be over-emphasized.

Holmes[4] reports that *G. kola* seeds are used as an antidote for *Strophanthus gratus* (a poisonous plant with strophanthin as its active constituent). It also serves as a remedy for guinea worm infection[5] and is used in the management of diabetes mellitus.[6] The flavonoid component of the *G. kola* seed which has been shown to have antimicrobial and anti-inflammatory properties,[7-9] consists of a single benzene ring joined to a benzo-pyrone structure and occurring in the free (aglycone) state or as 0- or C-glycosides.[10] The therapeutic value of flavonoids on the fragile connective tissue surrounding capillaries has been confirmed. For instance, they improve the connective tissue structure, which may lead to decreased capillary fragility and a reduced tendency for capillary contents to leak into the surrounding tissues. This implies that treatment with flavonoids may prevent oedema associated with inflammation and stasis.[11] Flavonoids such as disodium flavodate and trihydroxyethylrutin (troxerutin) have also been shown to be safe and effective for the treatment of chronic venous insufficiency.[12,13]

Flavonoids have been reported to effect a drop in adenosine triphosphate in venous endothelial cells during hypoxia. Consequently, this attenuates the inflammation response, the attraction of neutrophils, damage to the veins and the release of growth factors. These factors would normally perpetuate venous insufficiency and contribute to varicose veins.[14] Troxerutin, which significantly accumulates in both the inner and outer parts of the venous wall also displays an anti-erythrocyte aggregation effect and exerts a favourable action on blood fibrinolytic activity.[15] Furthermore, troxerutin totally inhibits the adherence of human unstimulated neutrophils to the endothelium of the umbilical vein when incubated in hypoxic conditions.[16,17]

The effects of the chronic ingestion of *G. kola* seed amended diet on the gastro-intestinal tract (GIT) motility in adult male rats was demonstrated by Braide, who reported that *G. kola* seed has an inhibitory effect on propulsive motility of the GIT.[2] Powdered *G. kola* seed diet when fed to rats for about 4 weeks (10% w/w) was seen to cause some histological alterations in the normal histology of the rats' liver, kidney and intestine. In the liver, most of the parenchyma cells were seen to contain small, but numerous cytoplasmic vacuoles. In the kidney, there were mild hydropic degenerative changes to cells of the proximal convoluted tubules while the duodenum exhibited epithelial cell vacuolation and showed evidence of detachment of the villus epithelium from the underlying stroma.[19]

Despite the fact that *G. kola* is used extensively in herbal medicine, and the seed is widely consumed in sub-Saharan Africa, including Nigeria, there is a dearth of published literature elucidating the physiological effects of this increasingly important edible seed, especially its activity on immune cells such as leucocytes in mammals like Wistar rats. It is hoped that this present study will shed more light on the effects and implications of the active ingredient (flavonoid) of the *G. kola* on immune cells, particularly the leucocytes of mammals, which will serve as a guide for its general use by the populace.

MATERIALS AND METHOD

Experimental Procedure

Ninety male Wistar rats, with an average weight of 200g, were randomly divided into three groups (A, B, C) of 30 rats each. Each rat in each group received 20g average consumption rate per day of 20%, 30% and 50% w/w equivalent of the ethanol extract of *G. kola* seed prepared diet, which contains 0.19g/kg, 0.28g/kg and 0.4g/kg, respectively, for two weeks. The first set of ten rats from each group (A1, B1 and C1) was sacrificed at the onset of the treatment and their determined values served as the control for their respective groups. At the end of each week, ten more rats were sacrificed from each group and they were tagged subgroups A2, B2 and C2 for the first week and subgroups A3, B3, and C3 for the second week.

Ethanol Extract of *Garcinia kola*

The *G. kola* seeds were collected from Rivers State, Nigeria, where they are widely grown. Four kilogrammes of the peeled seeds were sliced and pulverized with an electric blender and then air dried in the laboratory at room temperature (25° - 28°C). The dried kola was defatted using light petroleum ether (bp 40-60°C) in a soxhlet extractor for 24 hours. The marc was dried and repacked and then extracted with ethanol. The extract was concentrated and slowly dried over a water bath.

Preparation of Diet

The diet used for the study was composed of standard animal feed (Pfizers' starter mash) mixed with the ethanol extract of *G. kola* seeds in the following manner. A carefully weighed 9.4g, 14.1g and 23.5g of ethanol extracts of the powdered seed were dissolved in 500 ml of ethanol, respectively. The solution was mixed respectively with a binder consisting of 10% w/w ground cassava tubers; 980.6g, 975.9g and 966.5g standard feeds were carefully measured and gradually added into the corresponding solution of binder and extract, and thoroughly mixed. It was then moulded into small pellets and dried separately in an oven at a temperature of 40° C.

Blood Sample Collection and Analysis

Blood samples were collected by cardiac puncture while the rats were anaesthetized with chloroform. Two (2) ml of blood were drawn from each of the control rats at the onset of the study and at the end of the first and second week. On analysis, the leucocyte count and differential white blood cell count values were determined based on the method described by Schalm et al.[18] The mean values of the indices and the standard errors of mean were calculated. The values obtained were compared with that of the control values, and the standard-T test from

Stat works 1–2 software package (STAT Incorp., USA) was used to compute the level of significance, which was preset at $P < 0.05$.

RESULTS

The results of the haematological analysis for the treatment groups obtained at the end of the first and second week are presented. The mean values and the significant level of leucocyte count and the differential white blood cell count values for groups A, B and C are shown in tables 1, 2 and 3. The mean value of the leucocyte counts for all the treatment groups was significantly reduced at the end of the first week ,with the exception of subgroup B2, but at the end of the second week, after the *G. kola* administration, all treatment groups showed significantly reduced values ($P < 0.05$) when compared with their respective control groups. The differential white blood cell count showed variations in the values of the neutrophil, lymphocytes, eosinophil and monocytes in the treatment groups. These variations, however, were not significant ($P < 0.05$).

Table 1. WBC count and differential WBC values for group A

Variable	Group A1 N = 10	Group A2 N = 10	Group A3 N = 10
WBC count (10^9)	16.9 ± 0.8^a	12.2 ± 1.6^b	12.2 ± 0.5^c
Neutrophil (%)	30 ± 8.1	22.0 ± 7.0	27.5 ± 10.6
Lymphocyte (%)	67.7 ± 7.6	76.3 ± 12.0	69 ± 12.7
Eosinophil (%)	0.57 ± 0.9	3.67 ± 2.1	0.5 ± 0.7
Monocytes (%)	1.14 ± 0.8	0.33 ± 0.5	3.0 ± 1.4

A, B, C are significant at P < or > 0.05.

Table 2. WBC count and differential WBC values for Group B

Variable	Group B1 N = 10	Group B2 N = 10	Group B3 N = 10
WBC count (10^9)	16.95 ± 0.8^a	15.9 ± 2.3	10.4 ± 0.8^b
Neutrophil (%)	28.7 ± 8.6	23 ± 6.5	23.5 ± 2.1
Lymphocyte (%)	68 ± 8.0	73.6 ± 8.3	75.5 ± 3.5
Eosinophil (%)	1.43 ± 1.1	3.0 ± 3.0	0.5 ± 0.7
Monocytes (%)	1.28 ± 1.2	0.33 ± 0.5	0.5 ± 0.7

A, B, C are significant at P < or > 0.05.

DISCUSSION

The leucocyte and differential white blood cell count values obtained, following the administration of ethanol extracts of *G. kola* seed in the three groups of Wistar rats revealed variations in the values obtained at the end of the first and second week. It was observed that the white blood cell count of the entire test group decreased progressively at the end of the first and second week. However, the reduction in subgroup B2 was not significant ($P < 0.05$). On the other hand, the reduction in groups C, B2 and A was significant when compared with the control group values. These variations may be due to alterations in the rate of production of the various leucocyte pools, which might have been initiated by the biflavonoid content of *G. kola* seed. This corroborates the reports of other research[7,8] which suggests that *G. kola* possesses some anti-inflammatory and antibiotic properties. It has also been reported that leucopoenia may follow the use of antibiotics like chloramphenicol, penicillin and Dapsone.[20,21] Therefore, the reduction in the white blood cell count recorded may be due to leucopoenic activities of the anti-inflammatory and antibiotic properties bioflavonoids of *G. kola*.

Table 3. WBC count and differential WBC values for group C

Variable	Group C1 N = 10	Group C2 N = 10	Group C3 N = 10
WBC count (10^9)	15.6 ± 1.5^a	12.1 ± 1.6^b	7.8 ± 1.0^c
Neutrophil (%)	26.1 ± 5.3	18.3 ± 2.1	24.5 ± 10.6
Lymphocyte (%)	70.7 ± 7.4	79.3 ± 3.2	62.5 ± 1.4
Eosinophil (%)	2.28 ± 2.7	2.0 ± 1.0	2.0 ± 1.4
Monocytes (%)	0.85 ± 0.8	0.33 ± 0.5	2.5 ± 2.12

A, B, C are significant at P < or > 0.05.

The differential in the white blood cell count showed that all the variations in the values were not significant ($P < 0.05$), though there was a decrease in the neutrophil level in the peripheral blood. The decrease occurred at the end of the first and second week in groups A, B and C. Since these variations were not significant ($P < 0.05$), it probably suggests that these variations might not have been initiated by the biflavonoid component of the *G. kola*.

Other evidence implies that biflavonoids like trihydroxyethyrutin and disodium flavodate do not affect neutrophil phagocytic ability but, decreases oxidative tissue damage by neutrophils. This is facilitated by decreased reactive migration caused by the reduced reactive oxygen production.[11] Jain, et al.[21] also reported that certain antibiotics showed a significant reduction in the neutrophil chemotactic factors (NCF) and reactive

oxygen species (ROS). Martin et al[23] demonstrated that antibiotics in lower concentrations markedly depressed the migration of human leucocytes.

This study has shown that the biflavonoid constituent of *G. kola* seed has some anti-inflammatory properties and can exert some suppressive effect on white blood cell production. Therefore, its use in the treatment of potentially immune suppressive disease(s) should be regulated to avoid complications arising from excessive immune suppression.

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A demographic analysis and general health survey of suspects in police custody, Akwa Ibom State

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SUMMARY

There is a growing concern with respect to the increasing number of mentally ill inmates remanded in custody. The lack of a sound mind and reasoning, may predispose persons to commit crimes/antisocial acts, and oftentimes, many are sentenced with no recourse to their mental status.

The objective of the study was to determine the sociodemographic profile and general health status of suspects remanded in custody.

One thousand three hundred and thirty-one (1331) suspects, arrested and detained between January and June 2005, were surveyed to determine their general health status, using a 12-item general health questionnaire (GHQ-12).

One thousand two-hundred and ninety (96.9%) suspects were evaluated, while 41 (3.1%) could not be assessed because they were hardened criminals. One thousand and thirty-two (80.0%) were men and 258 (20.0%) were women; 1041 (80.9%) were 49 years and below; while 246 (19.1%) were 50 years and above. The mean age of the suspects was 36.4 ± 3.9 years.

A total of 789 (61.2%) suspects had secondary school education and below; 247 (19.1%) completed some level of tertiary education; 254 (19.7%) had no formal education; 429 (33.3%) were unemployed; 733 (56.8%) were married; 218 (16.9%) were single and 339 (26.3%) were either separated, divorced or widowed.

Reasons for arrest and detention varied: 402 (31.2%) were for traffic offences; 506 (39.2%) for assault; 100 (7.6%) for drug-related offences; 21 (1.6%) for advanced-fee fraud; 47 (3.6%) for child abuse/human trafficking; 120 (9.3%) for theft; 17 (1.3%) for rape/sexually-related offences; while 48 (3.7%) and 29 (2.2%) were for manslaughter and murder, respectively.

One hundred and ninety five (15.1%) scored equal to and above 3 on the General Health Questionnaire (GHQ-12) and were regarded as 'caseness' (psychiatric illness).

Mental illness is common among offenders and may be responsible for the increasing rate of crime in our environment. There is need for a routine psychiatric assessment of suspects to prevent the unjust punishment of offenders with mental illness.

INTRODUCTION

Mental illness is a major contributory factor to criminal activities in both developed and developing countries.[1] Crime is a socio-culturally-defined concept with serious consequences to the victims, and the perpetrators when apprehended.

A number of factors are responsible for the difficulty in determining the prevalence of psychiatric disorders, particularly in remand populations. In addition to the selective process of criminal prosecution and imprisonment, alternatives to prosecution and the manner in which specific psychiatric disorders are associated with criminal acts are possible known causes.[2] However, there has been an increase in the number of cases reported of psychiatric disorders in remanded prison populations.[3,4,5] Surveys have shown that the number of individuals with

psychiatric problems in prisons is greater than in the general population.[6,7]

The relationship between crime and mental disorders are influenced by factors such as the rate of crime, the operation of the criminal justice system, social policy in respect of the offenders and provision of health and social care for mentally troubled persons.[8] It has been observed that mentally ill offenders are more likely to be arrested and charged.[2] Although, various studies have associated an increase in the crime rate with mental illness, the high prevalence of psychiatric morbidity in prisons is not to be necessarily linked to criminal acts.[9,10] The arrest and trial process, as well as incarceration in a subhuman environment could result in high level of stress with mental decompensation.[5] Criminal behaviour, especially violence by the mentally ill is common and a major public concern. In addition to frustration from poverty and unemployment, violence contributes significantly to the high rate of offenders in prisons.[8]

Mental disorders which cause a certain level of disorganization and distortion in the reasoning process, often predispose the sufferers to a series of antisocial acts and behaviour. Offences such as theft, sexual misdemeanours, drug offences and murder are known to be associated with mental illness.[2] Several reasons, including lack of social support, resources and negative childhood experiences are believed to contribute significantly to these crimes.[1]

Criminal acts are also reported to be common among individuals with alcohol and substance abuse problems.[1,5,11] The impact of alcohol and substance abuse-related conditions are complex and endemic among offender populations.[3,5] The dysfunctional and unorganized aspects of the users' life often lead to crime. Alcohol consumption has been implicated in family violence, child abuse, rape and other sexual offences.[12,13,14] The occasional eruption of violence and aggression is high among alcohol and psychoactive substance users, and this would certainly have a negative impact on crime rate.[8]

In recent times, there has been an increase in the wave of violent crime among young people, such as rape, aggravated assault by cult members and murder in both the junior and higher institutions of learning. Many of these has been attributed to the effects of alcohol and substance abuse.[1] Factors such as reduced inhibitions, delirium tremens, hallucinosis, blackouts and amnesia are some of the underlying effects predisposing the users to risk-taking behaviours.[1,8]

Varying degrees of criminal behaviour have also been reported in women. Women in remand homes show high rates of neurotic conditions, personality disorders and substance abuse.[2,15] Drug-related offences, theft and fraud have also been reported to be common crimes among women.[16] However, women are less likely to be arrested for violence and burglary than men.[2] Persons who are mentally ill generally face intense problems while under the care of law enforcement agents. The lack of medical attention puts those who are unstable and whose reasoning is disordered in danger of being wrongly accused or even confessing to what they did not do. They are also less able to defend themselves in a court of law. These are the major handicaps that often expose them to unjust trials and punishment.

Although cases of detained suspects in remand custody abound in our environment, little is known of the general well-being and psychological status of these persons awaiting trial. This study, therefore, is aimed at examining the general health status of suspects. It is hoped that the findings would have a wider implication for mental health policy formulation and practice, with respect to the discharge of justice and an improvement in mental health services to the offenders.

MATERIALS AND METHODS

Location of the study

The study was carried out at three police stations in Uyo, Akwa Ibom State, Nigeria. Uyo as a capital city, attracts people from diverse cultures. It has an estimated population of 1.1 million people (1991 national census). There are four police stations, including the police headquarters, serving the entire city and its immediate environs.

Data collection

A total of 1331 suspects, detained in three police stations in Uyo between January and June 2005, were screened to determine their general health status, using a 12-item general health questionnaire (GHQ-12).[17] A semi-structured sociodemographic questionnaire was used to elicit information on variables such as sex, age, educational level, marital status, occupation and tribe. The GHQ-12 is a short version of the general health questionnaire designed as a self-administered screening instrument, aimed at detecting psychiatric disorders among respondents in community and non-psychiatric settings, such as primary care and general out-patient clinics. The GHQ-12 has been demonstrated in many

studies to have a high correlation coefficient with standardized psychiatric instruments.[18,19] The GHQ-12 is just as reliable, valid and sensitive as the longer version, but takes very little time to complete. The GHQ-12 has been used in many countries, including Nigeria.[1,20] It was used in this study because it was easy to administer and score, as it contains only 12 questions. Scoring was done by the conventional GHQ scoring method of 0-0-1-1, where positives indicate health and negatives indicate illness. All subjects who scored 2 and above were regarded to have psychiatric disorders. The cut-off point of 2 and above was derived from previous studies.[1,20]

Each of the police stations was visited twice a week throughout the period of study and eight assistants were recruited to help in the study. During each visit, all new suspects arrested and detained were given the general health questionnaire to fill. The questionnaire was also translated into the local language (Ibibio) and was administered to those with little or no education. All those with a history suggestive of past or present psychiatric illness were excluded from the study. The reasons for the arrest of each suspect were extracted from the charge register kept with the police in all the stations.

The permission to carry out the study was obtained from the Ethical Committee of the University of Uyo Teaching Hospital and the Nigeria Police Force. The study was anonymous and the police cooperation was strongly solicited .

Data Analysis

The results of this study were analyzed using Statistical Package for Social Sciences (SPSS 10.0). The proportion of the general health score was computed from the respondents. Sample means and percentages were calculated, from which simple frequency tables were created. The standard deviation from the mean was also calculated.

RESULTS

Of the 1331 suspects arrested, 1290 (96.9%) were assessed, while 41 (3.1%) were eliminated because they were inaccessible, being hardened criminals.

Table 1 shows the sociodemographic characteristics of the suspects. One thousand and thirty-two (80.0%) of the suspects were men and 258 (20.0%) were women; 1044 (80.9%) were 49 years and below, while 246 (19.1%) were 50 years and above. The mean age of the suspects was 36.4 ± 3.9 years.

Two hundred and fifty-four (19.7%) of the suspects had no formal education; 377 (29.2%) had primary; and 412 (31.9%) had secondary school education, while 247 (19.1%) had post secondary school education and above. A total of 429 (33.3%) were unemployed; 332 (25.8%) were employed, with 144 (11.2%) self-employed and 539 (41.1%) farmers or traders.

Seven hundred and thirty-three (56.8%) were married, 218 (16.9%) were single and 339 (26.3%) were either separated, divorced or widowed. Eight hundred and eighty-two (68.4%) of the suspects were indigenes of the state; 390 (30.2%) were from other parts of Nigeria, while 18 (1.4%) were non-Nigerians.

Table 2 shows the various crimes/offences and the number of suspects involved. A total of 402 (31.2%) suspects were arrested for traffic offences; 506 (39.2%) for assault; 100 (7.6%) for drug-related offences; 21 (1.6%) for advance fee fraud; 47 (3.6%) for child abuse and human trafficking; 120 (9.3%) for theft; 17 (1.3%) for rape/sexually-related offences; while 48 (3.7%) and 29 (2.2%) were arrested for manslaughter and murder, respectively

Table 3 illustrates the GHQ profiles of the suspects. One hundred and ninety five (15.1%) of the suspects scored equal to or greater than 2 on the general health questionnaire (GHQ-12) and these were regarded as 'caseness' (psychiatric morbidity).

DISCUSSION

The results of this study show that the suspects are predominantly unemployed; about 61% of them having secondary school education and below. This is similar to reports in previous studies.[7,21]

The twin social problems of unemployment and poverty can be intrinsically alienating and distressing; the direct and indirect impact on the development and maintenance of emotional, behavioural and psychiatric problems is daunting.[22] Crime is a man-made phenomena necessitated by several factors.[2] Although, 19.1% of the suspects had university education, the high rate of unemployment experienced due to economic recession, is a real threat that could drive even the most educated person into crime. Although many individuals may have completed secondary school, they lack employable skills, which constitutes a major barrier to employment; an individual unable to fulfill his day-to-day respon-

sibilities to his familyand peers may eventually turn to crime. This could result in increasing crime rate and other antisocial activities.

Table 1. Sociodemographic characteristics of the suspects

Socio-demographic variables	M ale		Female		Total	
	(n)	(%)	(n)	(%)	(n)	(%)
	1032	(80.0)	258	(20.0)	1290	(100)
Age in years						
• < 20	38	(3.7)	13	(5.0)	51	(4.0)
• 20 - 29	364	(35.3)	68	(26.4)	432	(33.5)
• 30 - 39	222	(21.5)	104	(40.3)	326	(25.3)
• 40 - 49	191	(18.5)	44	(17.1)	235	(18.2)
• 50- 59	153	(14.8)	19	(7.4)	172	(13.3)
• > 60	64	(6.2)	10	(4.9)	74	(5.7)
Educational level						
• No formal education	205	(19.90)	49	(19.0)	254	(19.7)
• Primary school	323	(31.3)	54	(20.9)	377	(39.2)
• Secondary school	311	(30.1)	101	(39.2)	412	(31.9)
• Post secondary school	139	(13.5)	37	(14.3)	176	(13.6)
• Post graduate	54	(5.2)	17	(6.6)	71	(5.5)
Occupation						
• Farmer	172	(16.7)	22	(8.5)	194	(15.0)
• Trader	226	(21.9)	109	(42.3)	335	(26.0)
• Unemployed	376	(36.4)	53	(20.5)	429	(33.3)
• Self-employed	115	(11.1)	29	(11.2)	144	(11.2)
• Employed	143	(13.9)	45	(17.4)	188	(14.5)
Marital status						
• Unmarried	163	(15.8)	55	921.3)	218	(16.9)
• Married	611	(59.2)	122	(47.3)	733	(56.8)
• Separated	82	(8.0)	28	(10.9)	110	(8.5)
• Divorced	61	(5.9)	19	(7.4)	80	(6.2)
• Widowed	115	(11.1)	34	(13.2)	149	(11.5)
Tribe						
• Indigenes (Ibibio and Annang)	678	(65.7)	204	(79.1)	882	(68.4)
• Ibo	162	(15.7)	21	(8.1)	183	(14.2)
• Yoruba	69	(6.7)	13	(5.0)	82	(6.3)
• Hausa	27	(2.6)	-		27	(2.1)
• Non Nigerian	15	(1.5)	3	(1.2)	18	(1.4)
• Others	81	(7.9)	17	(6.6)	98	(7.6)

Table 2. Various crimes and the number of suspects involved

Crimes	Male		Female		Total	
	n	(%)	n	(%)	n	(%)
Traffic offences	325	(31.5)	77	(29.9)	402	(31.2)
Assault (fighting and thuggery)	383	(37.1)	123	(47.7)	506	(39.2)
Drug-related offences	89	(8.6)	11	(4.3)	100	(7.8)
Advanced fee fraud (419)	21	(2.0)	0	(0.0)	21	(1.6)
Child abuse and human trafficking	19	(1.8)	28	(10.9)	47	(3.6)
Theft (including stealing, burglary and armed robbery)	106	(10.3)	14	(5.5)	120	(9.3)
Rape/sexually-related offences	17	(1.6)	0	(0.0)	17	(1.3)
Manslaughter	43	(4.2)	5	(1.9)	48	(3.7)
Murder	29	(2.8)	0	(0.0)	29	(2.2)
Total	1032	(100.0)	258	(100.0)	1290	(100.0)

Table 3. General health questionnaire (GHQ) profiles of the suspects

Score	Male		Female	Total	
	n	(%)	n (%)	n	(%)
One & below (≤1)	858	(66.5)	237 (18.4)	1095	(84.9)
Two & above (≥2)	174	(13.5)	21 (1.6)	195	(15.1)
Total	1032	(80.0)	258 (20.0)	1290	(100)

This study reveals that among those involved in crimes, a significant number of them are not mentally sound, resulting in their being arrested and charged. In this study, 15.1% of the suspects arrested for crimes and other offences scored high on the general health questionnaire, implying that they were suffering from a psychiatric illness.

Interestingly, women were also found to be involved in various crimes, although the percentages were much lower. However, 1.6% of the female suspects scored high on the mental illness scale, implying possible mental disorders. This is similar to previous studies that have reported different rates of mentally-ill individuals among the offenders.[3,4] Although, there was no attempt to determine the relationship between crime and different psychiatric conditions, the findings are comparable to earlier reports, in its demonstration that psychiatric morbidity may not necessarily mean that mental disorder is synonymous with crime. The stress associated with arrest, incarceration and the trial process could result in emotional instability, leading to mental illness among those arrested.[2] Therefore, it may be unreasonable to conclude that one particular form of offence is the hallmark of a specific psychiatric disorder. Furthermore, criminal acts are common among persons involved in alcohol and substance use.[8,11,13] It has been observed that people who suffer from a mental disorder are also prone to alcohol and substance use.[14] Although, the results of this study did not elucidate the attributes of the offenders in relation to alcohol and substance use, it was discovered that poor education and unemployment may predispose individuals to substance use/abuse, leading to crime and other antisocial behaviours.

Substance abuse, in addition to reducing inhibitions, also manifests in morbid conditions, which often result in risk-taking behaviours, including crime.[1] It is a fact that people with mental problems are often ignored and not given proper medical treatment, which could cause them to commit anti-social acts. This may be one of the reasons why many of them are more likely to be involved in acts leading to arrest and prosecution.

There has been increasing concern with regard to denying remanded suspects access to appropriate mental health care services. The policy makers and law enforcement agents are often unable to detect psychiatric problems among offenders. This is parlous and often lamentable, since it is ethically wrong to subject those with mental disorders and lack of competence, to routine court procedures.[2] The resultant effect is the violation of basic human rights of persons who are suffering from mental illness.

It would be appropriate to argue that those suffering from mental disorders have a diminished control over their thoughts and actions, hence, a significant number of them are involved in crimes and other antisocial activities. However, the usual act of feigning insanity by some criminals in order to escape justice for an offence

committed, poses a problem in determining the offenders with real psychiatric illness.

One of the limitations of this study was the inability to carry out a two-stage study to categorize the psychiatric symptoms, due to the regimentation and the nature of confinement of the suspects. The questionnaire was administered on every suspect arrested and detained, (except the 41 who were classified as hardened and were thus inaccessible). There was also some difficulty in determining the level of involvement of the suspects in various crimes, because the information on the crimes was based on police records.

CONCLUSION

The high scores of the suspects on the GHQ assessment scale is an indication that many may have been suffering from one form of mental disorder or another. The association between crime and mental illness is a clear evidence that an improvement in mental health services could help in reducing the high rate of crime in our society. In view of the foregoing, there is need to put in place appropriate policies aimed at catering for people with mental problems.

Efforts aimed at protecting persons with mental illness from being unjustly treated by the courts should be strengthened by liaising with mental health practitioners for routine mental examination of the offenders.

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Abortion-related morbidity and mortality in midwestern Nigeria

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SUMMARY

Induced abortion is one of the leading causes of maternal morbidity and mortality in Nigeria. While its contribution to maternal mortality has been previously reported for the big cities, little or no information exists for suburban and rural communities. In this paper, we assessed the magnitude of abortion-related complications, aimed at using such data to highlight the seriousness of the problem in our environment. A retrospective review of all cases of induced abortion managed at the Irrua Specialist Hospital, Irrua, over a period of seven years was done. Data analysis was carried out with SPSS statistical soft ware version 10.0.

Out of the 2894 gynaecological admissions during the period; 94 patients presented with induced abortion (3.25%). The patients were between the ages 16–38 years, with a mean age of 20.3 years. The majority of the patients (90.80%) were unmarried, nulliparous (85.10%), had less than tertiary education (66.6%) and never used contraceptives (89.7%). In 65 (74.7%) of the cases, the induced abortion was performed in a private clinic. The common presentations were lower abdominal pain (80.28%), fever (36.6%), vaginal bleeding (32.39%) and discharge (16.9%), anaemia (46.48%), septicaemia (14.10%), uterine perforation (5.6%) and septic shock (8.5%). Seven deaths were recorded from induced abortion, a case fatality rate of 8.1%; and 15% of the total maternal deaths recorded during the study period. Abortion-related morbidity and mortality is common and a major contributor to maternal morbidity and mortality in our society. The problem is bound to continue until strategies are put in place to reverse the high fertility rate, low contraceptive use and illegality of induced abortion.

INTRODUCTION

An estimated half a million women (worldwide) die each year during pregnancy and childbirth, of which 200,000 or more are due to botched abortions.[1] Induced abortion is one of the most difficult socio-medical problems facing our society today. This is so, because in a country where abortion is illegal, its magnitude cannot be estimated directly and its presence only comes to the fore when a case is complicated.

In Nigeria, unsafe abortion is responsible for about 20,000 deaths annually[2] and accounts for 27–77% of gynaecological admissions.[3,4] In a previous study on maternal mortality at this centre, abortion accounted for 15% of maternal deaths.[5]

Abortion–related morbidities and mortalities have been shown to have reduced appreciably in countries where abortion laws have been liberalized.[6,7,8]

A large number of abortions are undertaken everyday by those least qualified to do so, even though under the Nigerian law, abortion is illegal.[9]

This study was conducted to highlight the high mortality and severe morbidities associated with induced abortion in our rural communities, with the aim of drawing the attention of government and policy makers to this neglected scourge.

PATIENTS AND METHODS

The case notes of all cases of induced abortion seen at the Irrua Specialist Teaching Hospital (ISTH) between 1st

January 2001 and December 2007 were retrieved from the medical records department.

Data related to the socio-demographic profile of the patients, pertinent clinical features, treatment modalities utilized and outcomes were collected and analysed using SPSS for windows version 10.

RESULTS

A total of 2894 gynaecology admissions were seen during the 6-year period, of which 94 (3.25%) were cases of complicated induced abortion, which included 7 fatalities.

The socio-demographic characteristics of the induced abortion cases are shown in table1.

Table 1. Sociodemographic characteristics of patients with complicated induced abortion*

Sociodemographic characteristics	Number of patients	%
Parity		
• 0	74	85.1
• P_{1-2}	10	11.5
• P_{3-4}	2	2.3
• P_5	1	1.2
Marital Status		
• Unmarried	79	90.8
• Married	8	9.2
Educational Status		
• Primary	11	12.6
• Secondary	47	54.0
• Tertiary	29	33.3

* 7 fatal cases were not included in the data analysis in this table.

Their ages ranged from 16 - 38 years, with a mean age of 20.3 years. The majority of the patients (90.80%) were unmarried, nulliparous (85.10%), had less than tertiary education (66.6%) and never used contraception (89.7%). The presenting complaints among these patients were lower abdominal pain (80.28%), fever (36.6%), vaginal bleeding (32.39%), discharge (16.9%), collapsed (8.5%) and vomiting/diarrhoea (9.9%).

In most of cases, the induced abortion was performed in private clinics (65 – 74.7%) and patent medicine stores (13 –14.9%). Other places were maternity homes (8 – 9.2%) and private homes (1 – 1.2%).

Some of the methods used to achieve the abortion were dilatation and curettage 72 (82.8%), rupture of membranes and oxytocin stimulation 9 (10.3%), misoprostol 5 (5.7%) and native herbs and concoctions 6 (6.9%).

The complications among these patients are shown in table 2. Anaemia (46.48%), septicaemia (14.10%), uterine perforation (5.6%) and septic shock (8.5%) were the most common complications noted. Seven deaths were recorded (a case fatality rate of 8.1%); this accounted for 15% of the total maternal deaths seen in ISTH during the study period. Fifty-eight (61.7%) of the 94 patients presenting with induced abortion required surgical intervention. The common surgical interventions were laparotomy and evacuation of retained product of conception. All the 58 cases except one, had evacuation of retained product in addition to laparotomy. While 20(22.6%) had laparotomy and drainage of abscess, 5 (5.6%) and 6(7.0%) had repair of damaged bowel and perforated uterus. One patient required a subtotal hysterectomy because of the severely damaged and necrotic uterus.

Though a majority of the patients were aware of contraception (87.4%), only 10.3% had used any form of contraception. The types used were emergency contraception (5.6%), condom (3.5 %) and the pill (1.2%).

Table 2. Types and frequency of complications recorded among the patients

Complication of induced abortion	Number of patients	%
Anaemia	40	(46.5)
Septicaemia	12	(14.1)
Uterine perforation	5	(5.6)
Septic shock	7	(8.5)
Intestinal obstruction	5	(5.6)
Renal failure	4	(4.2)
Tetanus	3	(2.8)
Hypovolaemic shock	3	(2.8)
Fistula formation	3	(2.8)

DISCUSSION

This study, confirms a number of earlier studies, which have shown that induced abortion is an important gynaecological problem with serious socio-medical implications, and contributes significantly to maternal morbidity and mortality in our society.[3,4,7] The majority of these morbidities occur in young, unmarried women (91.55%); nearly 86% were nulliparous. The contribution of complicated induced abortion to maternal mortality in

this study (15%) is within the range (12 - 26%) reported in our environment.[11]

In the developed countries of Europe and North America, where abortion laws have been liberalized, abortion-related morbidity and mortality have become rare.[11] The reported low morbidity and mortality is not only related to the liberalization of abortion laws, but also to the introduction of sex education in schools and the social marketing of contraceptive commodities.[6,11]

The majority of these patients were young, nulliparous and single, showing that most of the victims of botched abortions were adolescents. Dr Okojie in Benin and Dr Anate in Ilorin reported similar socio-demographic characteristics.[12,13] It is instructive to note that 33.8% of the patients in this study are graduates of higher institutions. The message on safe sex is apparently not reaching its target audience. Adolescent-friendly family planning clinics are either not available or accessible to these young people. From this study, even though 87.37% had some knowledge of contraception, only 9.9% had ever used some preventive measures.

Because it is illegal nature, most abortions are done surreptitiously either in private clinics or patent medicine stores, where people, who are often the least qualified, carry out these procedures.[10, 14, 15, 16] Previous studies have shown that this could be attributed to cost, lack of knowledge and the illegal status of induced abortion. [2, 6, 12, 13]

The presentations in this study of lower abdominal pains with fever (36.62%) and vaginal bleeding (32.39%), are similar to previous studies in Nigeria and are largely due to infected retained products of conception. It may also be due to necrotic and/or perforated viscus.[10,11,14,15,16.] These complications are not unexpected, as the procedures were carried out in secrecy and with unsterilized instruments.[10, 12, 13]

The myriad of procedures carried out during the management of the patients is a pointer to the extent of damage done to these adolescents. The case fatality in this study suggests that the poor clinical status in which these patients usually present, and hence, the enormous contribution to the maternal mortality during the study period.

CONCLUSION

These figures are disturbingly high, particularly in a country where the fertility rate is high, contraceptive use is low and induced abortion is illegal. The tragedy of obtaining an illegal abortion and its associated morbidities and mortalities will continue to ravage young Nigerian women. More sex information must be made available to Nigerian girls and young women to enable them to protect themselves and avoid an unwanted pregnancy.

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Short Communication

Conducting clinical trials in developing countries: Experience from Tanzania

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BACKGROUND

There is no universal formula for starting, running or conducting a clinical trial. Whatever the approach, the trial must follow good clinical practices (GCP), time lines, and the accumulation of country-specific requirements. This means that, although the process of initiation, conducting the trial and closure must be followed, the approach will vary depending on the area, people and culture. In this paper, we documented our experience of conducting a multicentre clinical trial in Tanzania.

TANZANIA

Tanzania is an East African country with over 36 million people, the majority of whom live in rural communities. Its 120 ethnic groups are spread across 26 regions, with Dar es Salaam as the capital. It has a mixture of Christians, Muslims, indigenous religions, and a small number of Hindus. While the Muslims and Hindus are scattered across the islands and costal belt, the Christians and the adherents of the traditional religions dominate the rest of the country.[1,2,3,4]

The basic health infrastructures of the country are fairly well distributed, although they do not meet the needs of the populace.[5] The country has a potential supply of human resources, which could supply the needs of clinical research, however, only very few clinical trials have been conducted. The majority are either phase III or IV studies.

Approval of Clinical Research and Trials

The National Institute for Medical Research (NIMR), an agency of the Tanzanian Ministry of Health, is the agency usually saddled with the task of reviewing all applications for conducting clinical research in the country. Approval is also required from the Tanzania Food and Drug Agency (TFDA) in the case of trials which involve testing new products.

Institutional Review Board/ Ethics Committee

There are two types of institutional review boards; one deals with reviews relating to clinical trials (Clinical Trial Review Board), while the other deals with studies that are not clinical trials. An application for ethical approval must be submitted to the Clinical Trial Review Board before conducting any clinical trial in Tanzania. The study can only commence after the release of ethical clearance permit.

Clinical Trial Subjects

As the socioeconomic and educational status of the eligible trial subjects varies considerably, so does their understanding of clinical research. It is important, therefore, to spend considerable time and resources on advocacy and creating awareness, not only among the potential trial participants, but among the entire populace within the community hosting the trial. Experience from previous and on-going research trials has shown that community engagement right from the inception of the study, and throughout the trial, goes a long way in ensuring the timely recruitment of participants and their retention in the trial. Community awareness and understanding will also facilitate the resolution of any conflicts that may arise. Awareness is also needed among the medical staff, since they are also not very much informed about clinical trials.

Clinical Trial Investigators

Tanzania can draw from a large pool of human resource personnel to run clinical trials. Available human resources range from experienced researchers that have worked in previous trials — a majority of whom are staff of the National Institute of Medical Research, Tanzania and the inexperienced, new graduates from health institutions. The new graduates are normally very committed, however, sometimes it is difficult to recruit from this group, because most of them have not decided on career direction.

The specialties of these recruits vary from basic medical sciences to medicine and social sciences. Although a lot of qualified medical personnel exist, they are actively engaged in medical practices and usually do not have time for full clinical research. There is also a pool of biomedical and social scientists, however, experienced in running good clinical trials, however, their knowledge of good clinical practice are lacking.

For the successful conduct of trials in Tanzania, like anywhere else in the developing world, sponsors need to be prepared to invest heavily in building, improving and strengthening the clinical trial and good clinical practices knowledge before initiating the clinical trial.

CLINICAL STUDY SITES

Hospitals / Clinics

Tanzania has different types of hospitals, with different standards and ownership, and the quality and standard of care differ considerably. The ownership ranges from the government, private citizens to religious organizations. Hospitals owned by government are the most common. These hospitals are classified as referral, regional and district hospitals. In addition, within the government health care delivery system, are health centres and dispensaries. In each of these health institutions, the staff are overstretched by the heavy patient load, which makes it almost impossible for these health care workers to engage in clinical trials. It is therefore necessary to recruit additional staff to assist the institution's staff when conducting clinical trials in government hospitals. This will ensure that the old staff have time to participate in the study and still perform their primary functions. It is also important to train/sensitize the old staff before initiating any study.

Community

The Tanzanian community is friendly, with good and strong organizational structures. However, if you want to conduct a community-based clinical trial (e.g., study 13T), extra time should be allotted to sensitize the community, because it has a mixture of populations (illiterates, semi-illiterates and literates), with differing cultures, norms, religions and ethics.

Clinical Study Material

Most of the drugs/study materials for clinical trials are imported from abroad. The Tanzania Food and Drug Authority (TFDA) screens all materials imported for clinical trials. The TFDA insures that the rules and regulations concerning the importation of the drugs/trial materials into the country are followed. It also ensures the quality and safety of the drugs/materials.

Tanzania's customs authority requires a clearance certificate from TFDA before allowing any drug products into the country. An allowance of 4-6 weeks should be given for this process. After submission of the application, certain issues need to be clarified before the approval is finally given.

WORKING WITH NATIONAL PROGRAMMES

Ideally, it is better to work with national programmes, because it would be easy at the end of the trial to implement such study results into policy. Problems arise from the fact that the personnel in national programmes do not have experience in conducting clinical trials and therefore, additional staff would be required to assist the national programmes to run the trials.

There are several ways to ensure that the trial is successful. The first option is to build the capacity of the national staff in the running of a clinical trial and good clinical practices. The other option is to work in collaboration with research institutes which already have the capacity in clinical trials. A preferred approach will be a mix of the two options.

WORKING OUTSIDE NATIONAL PROGRAMMES

It is much easier to work outside the national programmes; opting to work with institutions that are experienced in clinical trials and have research infrastructures, eg, university/teaching hospitals or research institutes. The major challenge, however, is the translation of the trial results into policy.

CHALLENGES AND CONSTRAINTS

The leading challenge faced during the conduct of clinical trials in Tanzania is the low capacity of the staff on clinical trial conduct and good clinical practices. It is even worse if the research is nested within the national programme.

Finance is another major challenge in conducting clinical trials in developing countries, Tanzania inclusive. Conducting research with a large sample size and a long follow-up period becomes a major challenge. A large percentage of the budget goes to patient tracking, follow-up and transport refund. Training and retraining is also a major contributor to the high financial burden, as migration and brain drain of trained manpower constitute a major challenge.

Poor infrastructure is another big challenge, especially when the study is multi-centered, nested within a national programme or conducted in a remote area.

There could be bureaucratic bottlenecks especially if the trial is within a national programme and this could be caused by the difference between the scientist's objective(s) and the administrator's plans. These kinds of problems can delay the trial's progress.

Very often good and scientifically significant research results may not be translated into the policy of the country/ region where the trials have been conducted. The majority end up being published in journals or implemented in another country.

THE WAY FORWARD

Empowering scientists in good research methods through continuing medical education, the ethics of research and good clinical practices will simplify the conduct of trials in developing countries like Tanzania.

The medical/nursing schools should put more effort into training researchers; if possible, there could be a rotation through research institutes as a fulfillment of the candidate's qualification, like any other rotation in different departments like pediatrics, internal medicine etc.

For trials that will be embedded within the national programme, staff of different cadres in the programme should be given training in the conduct of clinical trials and good clinical practices before starting the study. Clinical trials should take into consideration the extra time needed to build the capacity of the staff.

In terms of budget, the coordinators should take into account the poor state of the infrastructure, as most institutions are ill- equipped. Likewise fluctuations in the exchange rate over time should be factored into the trial budget

CONCLUSION

Tanzania holds good potential for clinical trials, with a potentially good human resource base. The political stability of the country makes it an ideal place for research with long follow-up periods.

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