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Observation of Birth Asphyxia and Its Impact on Neonatal Mortality in Khulna Urban Slum Bangladesh

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Abstract Birth asphyxia and its impact on neonatal mortality were observed in Khulna urban slum during July, 2010 to June, 2011. The descriptive type of cross sectional study was conducted on 132 neonatal deaths among 9373 live birth. The study has found that neonatal mortality rate is 14 (n=132) in the study area compared to birth rate (9373). Of 132 neonatal deaths, birth asphyxia is responsible for 52(39%), low birth weight 32(24%), neonatal sepsis 22(17%), premature delivery 10(8%), developmental malformation 7(5%), neonatal jaundice 2(2%), acute respiratory infection 1(1%), and others 6(4%). Out of total live birth (9373) birth asphyxia was 266(2.83%), among them cured cases were 214(2.28%) and death was 52(0.55%). About 7961 under facilitate delivery in hospital/clinic, the neonatal death was 90(68%) and comprises birth asphyxia death was 30(33%). But in 1412 home delivery, the neonatal death was 42(32%) and the asphyxia death was 22(53%). Their knowledge on birth asphyxia due to lack of any institutional education (20%) or primary to high school level education (70%) and also the economic status ranges from 1500-2200BDT/month (44%) or from 2300-3000BDT/month (42%) may be the main risk factors which play an important role in neonatal mortality. The awareness of facilitated delivery rather than home delivery may improve the birth asphyxia death rate in Bangladesh and help to achieve the millennium development goal.
Keywords *Birth Asphyxia, Neonatal Mortality, Khulna Urban Slum and Millennium Development Goal*

1. Introduction

Globally, the neonatal mortality rate (NMR) is 36 per 1000 live births. Most of the 5 million deaths annually occur in developing countries, for which the NMR is 39 per 1000 compared with 7 per 1000 for more developed countries [1]. Millennium Development Goal 4, to reduce child mortality, sets a target of reducing the under-5 mortality rate (U5MR, the probability of dying by age 5 per 1,000 live births) by two-thirds by the year 2015 from a base line in 1990. This target requires that under five mortality rate (U5MR) decline on average by 4.4 percent per annum. The World Health Organization estimates that 38 percent of all under-5 deaths occur in the neonatal period .Of the estimated 130 million infants born each year worldwide, 4 million die in the first 28 days of life [2]. Three-quarters of

neonatal deaths occur in the first week, and more than one-quarter occur in the first 24 hours [2, 3]. Neonatal deaths now account for more than 2/3 of all deaths in the first year of life and for about 1/2 of all deaths in <5 children [4, 5]. Birth asphyxia is the failure to initiate and sustain breathing at birth (WHO, 2000). According to WHO, 2005 preterm birth accounts for 30% of global neonatal deaths, sepsis or pneumonia for 27%, birth asphyxia for 23%, congenital abnormality for 6%, neonatal tetanus for 4%, diarrhoea for 3%, and other causes for 7% of all neonatal deaths [3, 2, 6]. An estimated 1 million children who survive birth asphyxia live with chronic neuro developmental morbidities, including cerebral palsy, mental retardation, and learning disabilities [7]. Birth asphyxia is uses in hospital-based settings require evaluation of umbilical cord pH, apgar scores, neurologic clinical status, and markers of multisystem organ function [4]. Bangladesh has a neonatal mortality rate of 41 per 1,000 live births and neonatal deaths account for about 1/2 of deaths of <5 children [5]. Therefore, appropriate interventions are crucial for improving the health of <5 children in Bangladesh and to help achieve the global target of reducing <5 mortality by 2/3. Information on the timing and causes of neonatal deaths can help direct appropriate interventions. Bangladesh has a neonatal mortality rate of 41 per 1,000 live births and neonatal deaths account for about half of deaths of under-five children [5].

2. Materials and Methods

The study was a descriptive type of cross sectional study. The sample population of this study was newborn child mother, the cross sectional study was conducted by BRAC MNCH in Khulna urban slum under the city corporation. This study asses the neonatal death and proportion of this death in relation to birth asphyxia and socioeconomic status of the community. The sample size is 132 (neonatal death) among 9373 live birth in Khulna urban slum. The sampling technique was followed by non-randomized purposive sampling procedure. To find out the qualitative value interview and observation is appropriate technique. So, the data was collected from the interview of parents having the children last two years by using semi structured questionnaire. As a descriptive study, data was describing in frequency, tables and charts chi square. The study was carried out since April 2011 to October 2011.

3. Results and Discussion

3.1. Socio-Demographic Distribution of the Respondent

Respondent varies with age, education, and family status, 58% were of 21-30 age group, 23% were of 16-20 years age group, 21% (n=55) were of 31-35 years age group. Similarly among all the respondents 21.1% were illiterate, 41.3% had primary level education, 35.1% had secondary level education and 3.5% had higher secondary level education. Most of the family (77%) maintained single, followed by only 23% maintained combined family structure.

***Table 1**: Socio-Demographic Characteristic of Respondent*

Indicators	Percentage (%)
Age distribution (in years)	
16-20	23
21-25	18.3
26-30	39.7
31-35	21
Educational attainment	
Ever Been to school	79.3
Number of HH	
Highest level of education	
Illiterate	20.1
Primary	41.3

Secondary	35.1
Higher secondary and above	3.5
Number of HH	
Family status	
Single	**73**
Combined	**27**

3.2. Income Status

Income status varies with the geographical location, socioeconomic and political condition of the area. The study was found that 44% respondent income ranges from 1500-2200BDT and 42% respondent ranges from 2300-300BDT. The study revealed that who have higher income show lower neonatal death as they go for proper treatment during the neonatal period.

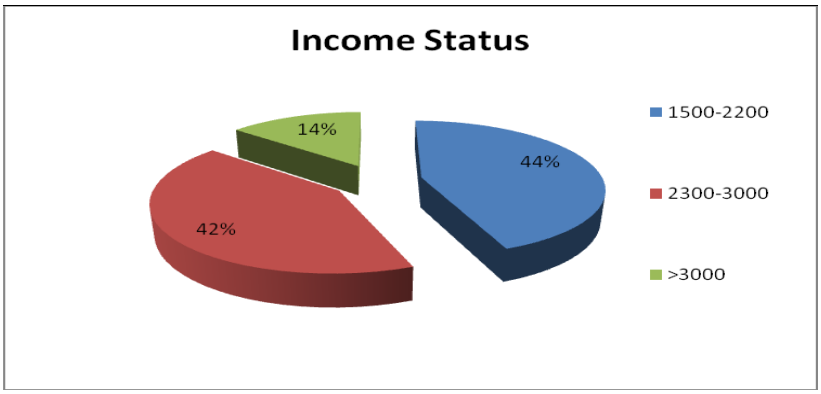

Figure 1: *Income Status*

3.3. Mode of Delivery

The study was conducted to define mode of delivery in relation to neonatal death. Mode of the delivery depends on some factors like socio-economic status, education and religion view of the people. The study was found that the normal delivery was more prominent (68.28%), where followed by c- section was 31.72%.

Table 2: *Comparison of Mode Delivery in Study Area (July'10 to June'11)*

Month	Jul' 10	Aug' 10	Sep' 10	Oct' 10	Nov' 10	Dec' 10	Jan' 11	Feb' 11	Mar' 11	Apr' 11	May' 11	Jun' 11	Total
NVD	480	544	604	631	684	645	503	439	518	471	436	453	6408
C /S	224	305	277	224	238	230	247	229	233	264	266	240	2977
Total	704	849	881	855	922	875	750	668	751	735	702	693	9385

Data Source (Field Survey, 2011)

A national study of neonatal morbidity in Bangladesh found that mothers who had ANC were more likely to seek care for sick neonates from a qualified practitioner, although most families sought care from homeopaths (38%) and village doctors (37%) who are mostly unqualified [12].

3.4. Cause behind Death

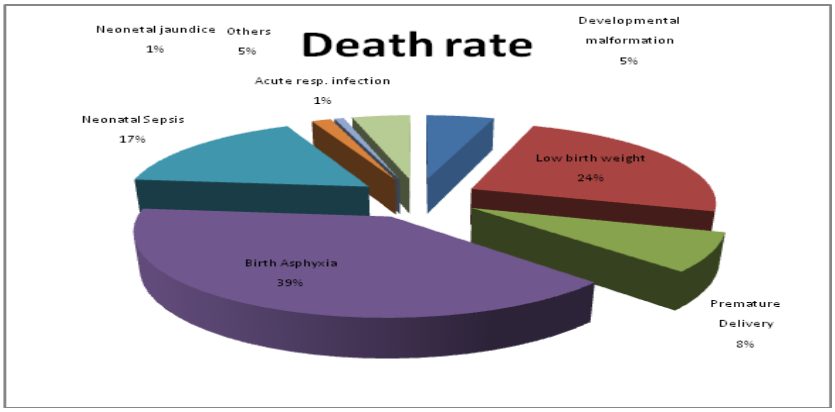

Figure 2: *Cause of Death*

The study has found that out of about 132 neonatal deaths birth Asphyxia is responsible for 52(39%), Low birth weight 32(24%), neonatal sepsis 22(17%), premature delivery 10(8%), developmental malformation 7(5%), neonatal jaundice 2(2%), acute respiratory infection- 1(1%), other- 6 (4%). Low birth wt. & neonatal species is another prominent cause for the neonatal child death in the study area. Similar type of study by Chowdhury was found the similarity data within his research, he has found that Birth asphyxia (44.9%), prematurity/low birth weight (15.1%), sepsis/meningitis (12.3%), respiratory distress syndrome (RDS) (6.9%), and pneumonia (5.5%) were the top five causes of death [8].

Department of Statistics, Biostatistics & Informatics Dhaka University stated verbal autopsy implicated birth asphyxia (as encephalopathy) in 34% of the cases, and infection (as either generalized sepsis or pneumonia) in 9% of neonatal deaths [9].

3.5 Comparison between Home Delivery & Facilitated Delivery in Relation to Neonatal Death

The study was found that home delivery and facilities delivery show different senior in the study area, it reveled from the study that home delivery represent the 2.97% of the child mortality against live birth and where facilities delivery shown 1.13% of child mortality against live birth.

Table 3: *Home Delivery and Facilities Delivery*

Month	Facilitate Delivery (Hospital/Clinic/DC)		Home	
	Live Birth	Neonatal Dead	Live Birth	Neonatal Dead
July -10	582	6	122	2
Aug-10	720	10	129	5
Sep -10	743	4	138	1
Oct -10	811	5	132	3
Nov-10	790	8	153	4
Dec -10	777	9	132	4
Jan -11	638	8	100	5
Feb-11	575	9	97	2

Mar-11	620	8	118	3
April-11	616	9	107	3
May -11	594	8	92	2
June -11	595	6	92	3
Total	**7961**	**90**	**1412**	**42**

Only 22(3.4%) of the 689 women who delivered at home had a qualified attendant (doctor, nurse, midwife or paramedic). Relative risk for neonatal death was lower, but not significantly [10].

3.6. Birth Asphyxia and Facilitated Delivery in Relation to Child Death

Birth asphyxia and facilitated delivery are interlinked; the study was like to disclose the relation to facilitated delivery and death of birth asphyxia. The study was found that neonatal child mortality rate is 1.39% (n=132) in the study are, compared to birth rate. It was disclosed that 7961 under facilitate delivery in hospital/clinic, the neonatal death was 90(68%) and comprises birth asphyxia death was 30(33%). But in 1412 home delivery, the neonatal death was 42(32%) and the asphyxia death was 22(53%). The same type of study by center for health and population research shown that direct causes were sepsis (32%), asphyxia (26%), tetanus (15%), respiratory distress (6%), others (6%), and unknown (14%) [11].

3.7. State of Birth Asphyxia

The study has found that medical facilities quite satisfactory in relation to birth asphyxia patient in the study area, it is clear from the study that about 80% birth asphyxia cured in the medical facility provided by the different medical institute of the Khulna city. The study expressed that out of total live birth (9373), total diagnosed birth asphyxia was 266 (2.83%) among them cured case was 214 (80.45%) & death was 52 (19.54%).

Table 4: *Status of Birth Asphyxia*

Birth Asphyxia	Jul' 10	Aug' 10	Sep' 10	Oct' 10	Nov' 10	Dec' 10	Jan' 11	Feb' 11	Mar' 11	Apr' 11	May' 11	Jun' 11	Total
Diagnosed	34	36	36	24	17	23	15	14	11	20	13	23	266
Referred	25	34	30	19	16	22	14	14	7	20	13	21	235
Cured	30	27	34	21	11	21	14	8	4	14	12	18	214
Dead	4	9	2	3	6	2	1	6	7	6	1	5	52

3.8. Causes behind Home Delivery

The study was found that education, income, easy access to clinic or hospital and religion belief play active catalyst to people not go for facilitated deliver at hospital or clinic during child birth. The substantial number (47%) of respondent uttered that, income status, followed by illiteracy (32%) and religion belief (22%) bind them in the home rather than facilitated delivery.

Table 5: *Cause behind the Home Delivery*

Causes	Percent (%)
Religion	21
Illiteracy	24
Income	25
Easy access to hospital or clinic	30

3.9. Child Mortality and Education in Relation

The study tried to link up a relation between maternal and paternal education in child birth and death, about 80% respondent's argued that education could play vital role in, eternal health care, less education, lack of knowledge & awareness about maternal health protection and care during pregnancy could cause the neonatal death. It was revealed from the study who have better education is more responsible and go for care during pregnancy and less child mortality also observed on those groups. The defined that, institutional education (20%) or primary to high school level education (70%) and also the economic status ranges from 1500-2200BDT/month (44%) or from 2300-3000BDT/month (42%) may be the main risk factors which play an important role in neonatal mortality. Department of Statistics, Biostatistics & Informatics Dhaka University stated in their study that mother's education exhibits a positive impact on child survival only for postnatal period. The proportion of children surviving beyond that period increases by 2.5 percent with a change in mother's education from none to primary. Similar results were observed for both wealth status and religion [9].

3.10. Schematic Diagram in Relation to Birth Asphyxia

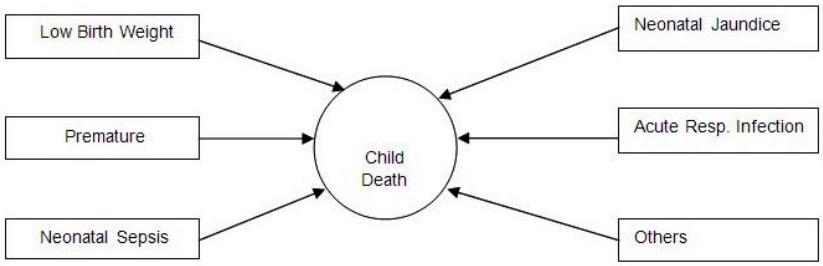

Figure 3*: Schematic Diagram in Relation to Birth Asphyxia*

3.11. Casual Loop Diagram of Child's Death

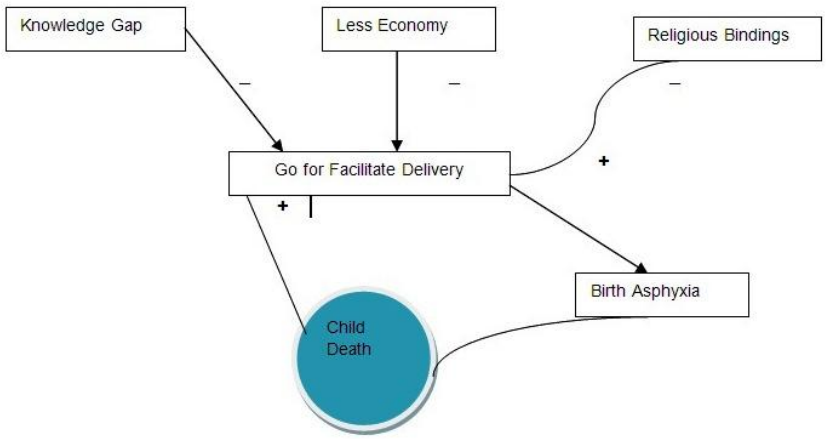

Figure 4: *Casual Loop Diagram for Death Rate*

4. Conclusion

Childhood mortality has strong relation to national development**.** It reflects level of socioeconomic development of a nation & quality of life. The present situation about neonatal care in Bangladesh indicates that much more has to be done to lessen neonatal health. Birth asphyxia is one of the main causes of the neonatal death in Bangladesh. As different factor are interlinked with the neonatal death by birth asphyxia, so we have to specify the cause of the death of birth asphyxia, by this connection should have to increased maternal care especially for the urban slum and rural population, awareness rising about facilitated delivery and safe delivery in hospitals and clinics so that death of the newborn babies could reduce by means of proper treatment. Need extensive research to identify the cause behind the Birth asphyxia and rather than socio-economic factor. Cooperation and combined efforts between the countries of the South East Asian region will help each other to improve the overall situation in the region. In this respect experiences of some of the countries who have improved neonatal care to satisfactory level will help other countries of the region. In this aspect need home and community based neonatal care which cause reduced the neonatal death by means of lowering the facilitated delivery.

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Review Article | Open Access

The Nutrition Profession in Africa: Meeting the Current and Future Challenges

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Abstract The relevance of nutrition to national development is very strategic; even though many sub-Saharan African countries do not consider nutritional challenges as critical. Poor disposition to nutrition in many African countries are aggravated by the quality of nutrition professionals in the region. There is lack of reliable information regarding the number of people working as nutrition professionals and the quality of the training received. Majority of countries in Africa cannot boast of world-class nutrition training institutes and linkages with standard foreign institutes are few. The dearth of highly qualified nutrition professionals has resulted into poor nutrition programme planning, implementation and evaluation. In some cases, the outcome of many nutrition intervention programmes is at variance with the set goals due to faulty programme planning and design. It is obvious that urgent consideration should be given to capacity building of nutrition professionals in developing countries, especially in those countries where the problem of malnutrition has remained unabated for many years. Developmental assistance from donor countries and other global bodies should have nutrition components. Capacity building in nutrition stands as one of the most cost-effective veritable tools to enhance national progress. However, the UNICEF's Conceptual Framework on the Causes of Malnutrition may need to include lack of capacity building for nutrition professionals as part of the strategies to tackle the underlying causes of malnutrition in developing countries. Availability of competent professionals in the field of nutrition may be the beginning of profitable journey to solving many problems confronting the continent of Africa.
Keywords *Nutritional Challenges, National Development, Nutrition Professionals, Capacity Building and Malnutrition*

1. Introduction

The abstract nature of nutrition as a field of endeavour does much to explain its poor image among other professions. Despite the importance of the profession to all aspects of national development, the nutrition profession has a poor status in many African countries [1]. The multi-disciplinary nature of

nutrition as a profession has made it vulnerable to usurping by professionals in related fields. At first glance, this might appear to be to the advantage of the profession, but the reverse is usually the case. Everybody feels associated with nutrition but few want to give better recognition to the profession and help with its development.

Poor understanding of what nutrition entails has contributed to some of the challenges confronting the profession at the national level. The inability of many national governments to distinguish between agriculture and nutrition is a major challenge. Moreover, many governments cannot distinguish between food and nutrition and, hence, much support is given to agriculture but little or none to nutrition programmes. The notion is that once food is produced, then, people will have enough to eat. However, food production is not synonymous with good nutritional status [2].

The issue of the brain drain is another serious challenge affecting the nutrition profession. Top quality nutrition graduates from Africa typically apply to universities or institutions outside Africa for graduate studies. Many of them do not return to their home countries after the completion of the studies.

Institutional capacity for training people in the field of nutrition in sub-Saharan Africa is very limited. Moreover, the quality of training is often technically deficient. It has been negatively affected by non-uniformity of curricula being used in various schools of nutrition. This has prevented students from acquiring similar basic knowledge in the field. As a result graduates from different nutrition institutions, with the same qualification – at least on paper – may display different levels of understanding of the subject. These differences in the curricula in schools of nutrition make the field of nutrition less professional! Some nutrition schools focus mainly on biomedical aspects of nutrition and do not include the social science components in their curricula. Graduates from such institutions will therefore find it very difficult to adopt social sciences approach to programme planning, implementation and evaluation. The likely aftermath of the deficiencies in training will include poor remuneration for some nutrition professionals who are working as civil servants. Another consequence of poor curriculum development is that nutrition professionals are often poorly qualified for leadership positions where they can be involved in policy development. As a result, very few nutritionists from countries like Kenya and Malawi have occupied political positions in African countries where they can be actively involved in policy development. Exposure of nutritional professionals to leadership training will assist in the development of competent nutritionists who will be skilled in policy issues and lobbying techniques to promote nutrition.

Some established institutions in Africa are beginning to see the problems associated with the shortage of nutritionists and are therefore embarking on some programmes that can assist in dealing with the problem. The field of nutrition has sometimes been treated as an “orphan”, without a domicile! For instance, in Nigeria, nutrition has been transferred between different government ministries; it was recently “finally” transferred to the Ministry of National Planning. However, another move is already in the offing to place nutrition directly under the presidency.

2. Continental Experience in Institutional Capacity Building in Nutrition

It is important to mention some experiences in Africa and some other developing countries with regards to institutional capacity building in the field of nutrition. Information obtained from the International Union of Nutritional Sciences (IUNS), United Nations University (UNU), and the African Nutrition Leadership Initiative Report of 1999 provides an in-depth historical perspective on this. For the last few decades several national, regional and international initiatives have drawn attention to the need for institutional capacity building in the area of food and nutrition, with a specific focus on developing countries. Since the establishment of the UNU in 1975, it has given highest priority to capacity building, especially in the south of Sahara [3].

A joint UNU and Administrative Committee on Coordination/Standing Committee on Nutrition (ACC/SCN) working group convened in 1984 to address the strengthening of institutions concerned with food and nutrition [3]. The working group recommended that high priority be given to the development of capacity of institutions that have the potential to become centres of excellence. The issue was further discussed at the IUNS meeting in 1989 held in Seoul, South Korea. The subject of institutional capacity building was the title of a workshop held by the IUNS and UNU in 1996. By 1997, it was reported that over 600 researchers and young scientists, over 40% of the UNU fellowships awarded, had received post-graduate training in the area of food and nutrition [3].

The results of institutional capacity building in Africa are of great concern as generally the impact of these initiatives has not been felt significantly in the continent that still plays host to high proportions of malnourished children and mothers in the world. Despite the reported fact that almost 27% of the UNU nutrition fellowships were awarded to people from Africa, only 1.5% of the fellowships were implemented at UNU-associated institutions in Africa. In 1988, a joint UNU and AAU (African Association of Universities) collaboration was initiated involving seven African countries, which aimed at strengthening national capacity in food and nutrition. However, the initiative was terminated in 1994 because an evaluation indicated limited impact on strengthening capacity for research and advanced training [3].

The Swedish International Development Agency (SIDA) has been involved in the strengthening of a number of food and nutrition institutions in Africa; for example, the Ethiopian Health and Nutrition Institute, the Zambian National Food and Nutrition Commission, the Tanzanian Food and Nutrition Centre, and the National Nutrition Unit of the Zimbabwe Ministry of Health and Child Welfare. The outcome of the experiences of Zimbabwe and Tanzania has been considered generally positive in some aspects of the capacity-building process [3].

There have been some forms of support from foreign institutions, one of which is the Applied Nutrition Programme (ANP) of the University of Nairobi, which was launched in 1985 with the support of the Deutsche Gesellschaft fur Technische Zuzammarbeit (GTZ), the German Agency for Technical Cooperation. Nearly 100 students from Eastern, Central, and Southern Africa have gone through the Masters of Science in Applied Nutrition programmes; trained by highly qualified professionals. The ANP serves as a good example of how to build up institutional capacity [3]. It is also important to mention the roles of some Europe and North America-based Universities in ensuring that budding talents in the field of nutrition from Africa are developed to build up the local capacities in the profession. These institutions include Wageningen Agricultural University in Netherlands, Emory in USA and Southampton in the UK among many others. The only challenge with these available opportunities has been that many of the trained African professionals prefer to stay back and pick up employment in the institutions where they were trained or seek for international jobs outside the continent resulting into loss of promising manpower and thereby defeating the main essence of the opportunity for the training, which is to build the local capacity of nutrition professionals! Presently, this problem has been partially controlled through partnership programme with some African Universities; as we currently have in countries including Benin, Ghana, South Africa, Tanzania, Zimbabwe and other notable Nutrition Institutes as in the Ethiopian Health and Nutrition Research Institute. The graduates are being mandated to return to their countries and work. However, the effectiveness of this approach has not been evaluated. Anecdotal information, however, reveals that more efforts on capacity building in nutrition have been directed towards the Eastern and Southern African countries than any other region in the continent.

While the efforts of institutional capacity building in Africa have generally not been evaluated to determine the success rate; similar initiatives in Latin America and Asia have been relatively successful. In these regions a number of key regional and national food and nutrition oriented institutions have been established in Central America and Panama, and Thailand. Available

opportunities for capacity building of African nutritionists in these institutions have not been explored. A number of lessons can be distilled from the experience of building or strengthening institutions from the developed world. The fundamental lesson learned has been that political will must exist. Government support is indispensable for any capacity building to be successful. Other essential ingredients include:

a) Development of a core group of professionals who are well trained, has multiple skills, and are highly motivated.

b) Availability of critical mass of well-trained people, with a strong and visionary leader, and long-term budgeting commitment from both the member countries and external financial contributors.

There is much variation in successive institution capacity building initiatives. However, it appears that in Africa success is more likely when the initiative is implemented at academic institutions than at government institutions [3]**.**

3. Current Situation of Capacity Building in Nutrition in Africa

There are very few bodies in Africa that are actively involved in building the capacity of young people and developing their leadership potentials. Of notes are the African Nutrition Leadership Forum, which is based in South Africa and Federation of African Nutrition Societies (FANUS) also plays vital leadership roles in promotion and capacity building in nutrition in Africa. These bodies have the capacity to train young leaders and exposure them to the field in order to be able to take well-informed steps in the development of policy. More national and international bodies with nutrition orientation and agenda need to be co-opted and sensitized to provide more support that will improve the training of nutrition professionals. Apart from the ANLP, others may need to do more in terms of playing a leadership role in the promotion and development of nutrition in Africa.

Other regional bodies are presently preoccupied with mainstreaming nutrition in the national development agenda. These include the Africa Nutritional Epidemiology Conference (ANEC), Information Technology in the Advancement of Nutrition in Africa (ITANA), Food Science Network for Africa (FOSNA), West Africa Health Organization (WAHO) and the Economic Commission of West African States (ECOWAS) Nutrition Forum. These bodies may need to look at providing assistance to both young and middle age graduates in acquiring training in certain vital areas, namely nutrition advocacy, communication skills, and governance. However, there has been some insinuations that middle age or older graduates are always more eager to return to their countries after the training than the younger graduates who may decide not to return after the training. This may be attributed to the fact that many of them have not established family ties who may serve as a pulling factor to return to their countries after the training.

3.1. The Need for Capacity Building in the Nutrition Profession in Africa

Nutritional problems around the world are rapidly evolving alongside changes in global socio-economic conditions and the interconnected nature of national economies, demographic transitions, and continued population growth. These rapid changes pose many challenges to human health. This creates much need for involvement by nutrition professionals. These professionals must be well-equipped to meet the needs of the fast-changing world. In the face of this development, investment in human and institutional capacity in the field of nutrition should be a priority [4]. Unfortunately, such investment has been inadequate and uneven in many regions.

There are critically important issues to consider in capacity building of nutrition professionals. The first is to ensure that the training is organized so that it makes a tangible difference in solving nutrition

problems. In addition, there is a need to build or strengthen institutions and in particular, it is vital that institutions are sustainable. A variety of approaches have may be suggested for advanced training leading to degree programmes in nutrition. For a successful outcome of institutional capacity building, good programme planning should be supported by setting clear and achievable goals.

In line with the above, research is the cornerstone of scientific and scholarly work and should be vigorously pursued as a component of capacity building. It is an essential component of any strategy that aims to improve the nutrition situation in Africa. However, the capacity of research institutions is generally quite weak across Africa [4]. One of the reasons for this is because many young nutritionists find it extremely difficult to publish their research findings in well-respected journals. Other barriers are limited access to scientific journals and the cost of internet services and payment for the publication of the accepted manuscript in a reputable journal.

One of the effective ways to build capacity is to develop partnerships with institutions in developed countries. Unfortunately, relatively few nutrition institutions in Africa have been successful along this line. Even where this has been accomplished, there is still a negative side to this as some of the trainees may be granted employment by the host country and this obviously does little to help with capacity building in Africa.

South Africa is the major exception to many of the above problems. That country has numerous high-quality universities and many highly respected nutrition professionals. It also has a highly commendable level of interaction between its universities and other institutions and partners in highly developed countries.

4. Strategies to Address Current and Future Challenges in the Field Of Nutrition

Meeting the challenges faced by the nutrition profession in Africa will require a great deal of work and this may include:

- Young institutions of learning need to collaborate with the older and more developed ones; and
- Regional bodies can enter into partnerships with established international bodies.

In addition, there is a great need for self-development efforts by people as individuals.

The following should be viewed as the key strategies in building the field of nutrition:

- Harmonization of the basic nutrition curricula in schools and colleges that run nutrition programmes.
- Setting up of a minimum standard to qualify as a nutritionist.
- Developing a strong advocacy for nutrition through lobbying the political stakeholders.
- Defining the main roles for nutritionists within the context of the national civil service.

It should be noted that in facing current and future challenges, there is a need for adequate training in the following key areas: nutrition advocacy, development of communication skills, nutrition programme planning, implementation, and monitoring and evaluation.

In order to advance this agenda and advocate for nutrition promotion there is a need for a systematic approach to policy development and capacity building. This can be achieved through formal and informal meetings between concerned professionals and other stakeholders.

Nutrition challenges vary from country to country in Africa. Therefore, any approach to institutional building must be based on reliable information. This requires a situation analysis that provides information on institutional capacities and identifies areas that require strengthening, and determines the level of knowledge and skills, financial support, and physical assets.

5. Upgrading of Nutrition Education

The introduction of a uniform curriculum for nutrition programmes in schools will set the pace for uniform examinations for graduating students. This may ultimately usher in registration of successful students with the national nutrition board (or an agency mandated to register professionals in various countries).

The suggested uniform curriculum should include the courses listed below in addition to those that are specific to various institutions:

- Classes of foods, characteristics of foods
- Food science and technology
- Food safety and environmental health
- Ecology of food and nutrition
- Feeding practices of different age groups (lifecycle nutrition)
- Food and agricultural systems
- Ecology of health and disease
- Nutritional physiology and biochemistry
- Nutritional behaviour and social science aspects
- Nutrition-related disorders
- Nutritional assessment
- Nutrition and reproductive health
- Nutritional epidemiology – population level description of distribution of nutrition problems
- Clinical nutrition
- Introduction to Basic Economics Principles – micro and macro concepts
- Introduction to Political science
- Introduction to Human psychology
- Introduction to Anthropology
- Communication behaviour and Nutrition Education
- Ethical issues in nutrition research
- Nutrigenomics
- Research design/methods/interpretation, including epidemiological methods and nutrition surveys
- Basic statistics
- Health education approaches
- Management – programme planning, monitoring and evaluation
- Leadership attitudes and skills as part of programme management skills
- Communication, negotiation, motivation, collaborative problem solving, concepts, and skills
- Principles of reflective Nutrition/Dietetics practice
- Nutritional Concerns of National Security Agencies
- School Feeding and Nutrition Programmes
- Hospice Nutrition
- Introduction to international food culture
- Planning, Monitoring and Evaluation of Community/National Nutrition Programmes
- International Politics and Human Nutrition

- Nutrition in Emergency and Refugee Camps
- Nutrition and Millennium Development Goals
- Computer education/information technology

6. Building Research Capacity

There is a dire need for increasing research capacity. In this regard, the principal objectives may include:

- Strengthen the ability to respond to national and regional research needs
- Increase the proportion of nutrition research conducted by national or regional institutions, and
- Identify, focus and find solutions to the nutritional problems of most national and regional significance

With adequate planning and mobilization of relevant resources, it is possible to achieve all these set of objectives. Clear understanding and involvement of all the stakeholders in developmental agenda, especially the political bigwig will promote efforts towards capacity building in nutrition research. This should be fostered by investment in establishing standard institutions to promote cutting-edge researches and provide the enabling environment for manpower training for future nutrition programmes in Africa.

However, it is envisaged that if all the institutions presently running nutrition programmes in Africa are to be given the opportunity to present candidates for training opportunities in some of the world class institutions outside Africa; or if some resources are made available for such programmes, it can never be enough. Since resources for training and development of manpower in the field of nutrition are inadequate, the little available should be judiciously utilized. Therefore, it becomes very necessary to develop criteria that can be used for the selection of highly qualified professionals or institutions that will be supported from such limited available resources. These criteria may include good track record of the professionals (usually determined by number of research publications, years of working experience and involvement in collaborative researches, etc.), and/or the institutions concerned (e.g. academic standard of the institutions determined by global rating of the institution), the strength of the local national nutrition bodies (e.g. fully registered and recognized body by the national government, affiliation to regional or continental body and evidence of linkage with international institutions in terms of research or other forms of partnership) and some evidence of national government commitments to nutrition, which can be determined by finding out if nutrition is instituted as a separate body/unit among many agencies of government or if it is not recognized in the national scheme of things. Furthermore, research centres/institutions that will be chosen for capacity building must have a multi-disciplinary orientation, in keeping with the standard of disciplines required to address most nutrition problems, while at the same time each unit in the nutrition department should develop its own area of specialization.

It should be reiterated that the nature of nutrition as a multi-disciplinary field should not be undermined within the context of capacity building in nutrition research. This brings to fore the need for graduate students to be very versatile and exposed to other disciplines that will position them to face any challenge in the course of solving nutrition problems. It is important for graduate students/researchers in the field of nutrition to create a niche of specialties from the beginning of their career so that they have an area of concentration to follow. However, in a developing world like many African countries, evidence-based researches and problem solving studies will be highly favoured as against basic researches, which may not be greatly valued at the present dispensation in many developing nations of Africa. Problem solving researches/studies in nutrition can actually be a good

social marketing strategy to create better support for the development of more interest and manpower in the field of nutrition.

The development of mentoring relationships and faculty exchanges is equally of much value as part of capacity building in nutrition research. Enhancing research capacity through the improvement of highly specific skills may be obtained through good mentoring process.

7. Dietitians and Nutritionists

The main focus of this paper has been on nutrition professionals in the broad meaning of the term. It is however, important to state that the challenges facing Africa with regard to nutrition professionals are more acute with respect to dietitians than for nutritionists in general.

Presently, in many African countries, nutritionists do not necessarily have a formal qualification in nutrition. Membership of national nutrition societies come from a variety of different professionals, including medical doctors, home economists, nurses, biochemists, and physiologists working in specialized areas of nutrition. Dietitians, by contrast, normally have a degree in nutrition and specialized training in an area of nutrition practice, such as clinical nutrition or public health nutrition. It is highly recommended that before anybody can claim to be called a nutritionist in Africa, the individual must have a minimum qualification of a diploma in nutrition. The present situation of nutrition as a profession in Africa may be traced to people who have never received any formal training in nutrition but teach the subject in higher institutions of learning or working in government establishments and non-governmental organizations as nutrition officers. These people may not have all the expertise required to move nutrition beyond the present status. In the contrary, Dietetics which is part of nutrition; appears to be better coordinated in Africa. This is because members have to undergo training with a uniform curriculum and certified by the national body before they are registered and allowed to practice.

It is important to note that Nigeria and South Africa are the only two countries from Africa that are members of the International Confederation of Dietetic Associations (ICDA) (http://www.internationaldietetics.org). By contrast, roughly 21 African countries do have an active nutrition society.

In conclusion, it is hereby re-emphasized that the survival of nutrition in Africa is hinged on sound capacity building, which goes beyond the frontiers of national government. It cannot be over-emphasized that nutrition is a vital part of national development agenda. The more equipped the capacity of the professionals in the field, the better it becomes for the national governments; who will benefit immensely from the expertise of these professionals. It is succinctly suggested, however, that the highly referenced UNICEF Conceptual Framework (UNICEF, 1990) [5] for causes of malnutrition may need to include capacity building of nutrition professionals as part of the underlying causes of malnutrition. National and international development programmes without due considerations for nutrition may not achieve their goals as expected and the time to build the capacity of the professionals in this field should not be delayed further.

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Socioeconomic Condition and Health Status of Chronic Arsenicosis Patients in Jessore, Bangladesh

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Abstract A descriptive type of cross sectional study was conducted in Sharshaupazila under Jessore district on socioeconomic condition and health status of chronic arsenicosis patients from July to October, 2011. The prevalence of arsenicosis due to arsenic contamination of ground water may emerge in the form of epidemic and chronic arsenic exposure through drinking water is one of the major environmental hazards in Bangladesh. The main source of drinking water is shallow tube well (64%) among which 21% tube well has been red marked i.e., contaminated with arsenic poisoning. About 59.8% respondents have belonged to income deficit group and their monthly income decreased significantly. The chronic effect due to arsenic poisoning is about 32% and the men (69.33%) were more susceptible to arsenicosis. Among the affected patients identified problems were melanosis (94%), keratosis (33%), leucomelanosis (38%), respiratory problem (49%), loss of sensation (45%), bowen's (21.33%), oedema (9.33%), chronic nonhealing ulcer (6.33%), lung cancer (2%), and gangrene (0.66%). About 32.94% people consulted with homeopath for their treatment and only 22.35% people consulted with government health physician. To be aware of arsenicosis the health education must be improved within the community and the financial support; relevant training could be effective to reduce the arsenic poisoning.
Keywords *Arsenicosis, Health Status and Socioeconomic Condition*

1. Introduction

Groundwater contamination by arsenic is one of the largest problems in Bangladesh; millions of people are being affected by the arsenic in recent past. Huge numbers of tube-well were installed to protect the people from waterborne diseases, but water of the tube-well not properly tasted about the contamination of arsenic. People who have long term exposure to arsenic contaminated water more than 500mg/liter may ultimately die from cancer caused by arsenic. Statistic shows that arsenic contaminant cause chronic causality like as lung, bladder and skin cancer. Statistic also shows that one in every ten people may fall in chronic diseases because of long term exposure of arsenic [1]. In Bangladesh source of drinking water is one of the largest exposure way to inorganic arsenic to human body [2]. People of Bangladesh are facing largest poisoning of arsenic in recent history, and millions

of people are drinking water with high level of arsenic which is above the permissible limit. Health catastrophe has gradually unfolding creating threat to the people of Bangladesh [3]. Arsenic also creating problem to child and maternal health, which cause spontaneous abortion and still birth [4]. In Bangladesh more than 60 districts are affected with arsenic by ground water contamination. Which cause future generation at great risk of arsenic contamination and statistic show that about 38430 identified patient existing in Bangladesh (BAMWSP, 2004). But the actual magnitude of the problem and upcoming future burdens very difficult to scale up and therefore this study us just an endeavor towards touching the tip of the iceberg in capturing the entire scenario in a single frame. There are two million cases of skin lesions in the country caused from drinking arsenic contaminated water and 3,000 people is dying every year in Bangladesh by arsenic-related illness. Disease resulted from chronic arsenic exposure is commonly known as arsenicosis. Early symptoms of arsenicosis include various skin lesions (cancers) that develop over an incubation period of 5-10 years of continuous exposure. After 10-20 years of prolonged exposure, afflicted persons often develop arsenic-related cancers. Although no specific treatment of arsenicosis has yet proved to be effective, patients experiencing arsenic poisoning tend to seek treatment from health professionals. Use of antioxidant multivitamins (vitamins A, C and E), various skin lotions and drinking arsenic free water have been shown to be beneficial in some extent for the people who are in the initial stages of arsenicosis. Eating selenium rich foods, such as fresh fruits, vegetables, eggs and milk also help to reduce the effects of arsenicosis symptoms. Arsenic patients who are in the advance stages may require surgical interventions if they suffer from gangrene and arsenic related cancers. WHO (1993) [5] listed the symptoms of arsenicosis roughly in successive order as changes of skin color (either hyper-pigmentation or de-pigmentation), skin and internal cancers, peripheral vascular disorders and neurological disorders. The liver and lung may also become affected. Arsenic poisoning also affects the productivity of the sufferers, and its debilitating nature may disrupt their family harmony. Although arsenic contamination of ground water was first identified in 1993, even now many of the people, who are drinking this contaminated water, are not aware of this fact and its consequences.

2. Materials and Methods

The study area is situated near about 35 km south-west from Jessore district and it was selected because of the study area is in a great risk of arsenic problem and more than 65% tube well of the area is red marked or highly arsenic concentrated. Study period was July to October, 2011. The chronic arsenicosis patients with the age range from 30- 69 years of old were including in this study. The people aged below 30 years and mentally retarded were excluded. Stratified random sampling was used as sampling procedure. Both qualitative and quantitative information has been collected by using semi-structure self-develop questionnaire. Information from 107 respondents was collected through interview. The sample size for data collection from each stratum was obtained from the following equation (Kothari, C.R., 2001):

$$n = \frac{z^2 pqN}{e^2(N-1) + z^2 pq} \qquad (3.1)$$

Where n = sample size; z^2 = the value of the standard variant at a given confidence level; p = sample proportion; q = 1-p; e = acceptance error; N = population size for the strata.

For the study, as the sample proportion would represent 25% of the population, thus the value for the equation is: p = 25% of the population, i.e. 0.25; q = 0.75; z = 1.96 [for 95% confidence level the value of z is 1.96]; e = 0.08 [since the estimate should be within 10% of the true value];

Therefore,

$$n = \frac{1.96^2 \times 0.25 \times 0.75 \times 2142}{0.08^2 (2142-1) + 1.96^2 \times 0.25 \times 0.75} = 107$$

Data collection tool was semi structured questionnaire. Data management and analysis was followed a sequential order. Secondary information such as statistical data, reports, has been collected from various government and nongovernment organizations. Demographic information such as household data was collected from Bangladesh Bureau of Statistics, Jessore. Social information from Upazila Parishad Office, Sharsha.

3. Results and Discussion

3.1. Socioeconomic Condition

Arsenic contamination is one of the most threatening health issues in Bangladesh, particularly in study area. Arsenic contamination causes health hazard and putting continuous pressure on sociology-economic conditions of the people. It is affecting the people in the study area not only physically but also economically, environmentally and socially. As a whole the area is under insecure condition both environmentally, economically and socially. To explain the socioeconomic condition of the study area the following socioeconomic criteria are considered.

Table 1: *Socio-Demographic Characteristic of Respondent*

Indicators	Percentage (%)
Age distribution (in years)	
<20	20.91
21-30	15.82
31-40	40.75
41-50	19.71
51-60	12.91
60+	6.34
Mean Age (in years)	29.91
Educational attainment	
Ever Been to school	78.4
Number of HH	**376**
Gender Distribution	
Female	58.82
Male	41.18
House type	
Earthen structure	95.30%
Semi brick structure	2.80%
Brick structure	1.90%
Highest level of education	
Primary	44.2
Secondary	52.7
Higher secondary and above	3.1
Number of HH	**376**

The analysis of the age group of the study area showed that, age group of 31-40 years is mainly engaged in income activities (40.75%), followed by 41-50 years (19.71%), 51-60 years of age groups are engaged (12.91%). These three age groups mainly constitute the main work force in the study area (73.37%). Although it does not show any significant relationship with their livelihood but only indicate that, the livelihood of middle aged category (31-40 years age) is more affected by arsenicosis. The total respondents of the study area were categorized into two groups according to

their sex. In general, there were more female than male respondents. Among them 58.82 % patient were female and 41.18% patients were male. The nature of house indicates the social status of the community people. People in the study areas generally use available local materials for construction of house. Depending on the wall materials the housing of the study area can be classified into three categories and these are earthen (materials of housing are mud, straw, bamboo, golpata) semi-brick (materials of housing are tin, asbestos, brick) and bricked. In this case most of the people have earthen structure house (95.30%), small percentage of the people use semi-bricked (2.80%) and brick structure house (1.90%).

3.2. Sources of Drinking Water

Source of drinking water is another important indicator of the socioeconomic condition for the people in the study area. The study showed the majority of the respondents obtained their drinking water from shallow tube-wells (64%) with nearly 29% using deep tube-wells, pond sand filter (2.5%), and traditional well (5%) respectively. The study results are similar with the results of Faruque et al. more than half (54%) regularly consumed well water with an as concentration ≥ 50 µg/L- above the acceptable government standard in Bangladesh due to lack of knowledge [6].

Table 2: *Source of Drinking Water*

Source of Drinking Water	Percent (%) of Respondent
Shallow Tube –well	64
Deep tube –well	29
Dug well	5
Pons sand filter	2

3.3. Location of Drinking Water Source of Respondents

The supply of water has always been a problem in Bangladesh. In the rural area, the source of drinking water is a great concern. The presence of arsenic in the underground water is another problem which is being intensified day by day. In the study area about 38.82% drinking water source were inside their houses and the rest of the households 61.18% collect drinking water outside their house. Out of this 61.18% source of water was more than that of 500 meter of the house. The distribution of the respondents based on the location of drinking water source is shown in the figure 1.

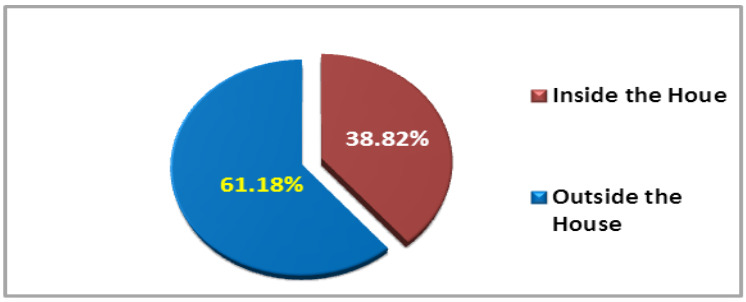

Figure 1: *Distribution of the Drinking Water Sources in the Study Area*

3.4. Perception about Arsenic Poisoning

The study was found that, the majority (73.15%) of the respondent had no basic knowledge about arsenic poisoning. Only 26.48% people had little knowledge about arsenic poisoning and 18.2%, 8.65% people had little and medium knowledge, respectively about arsenic poisoning.

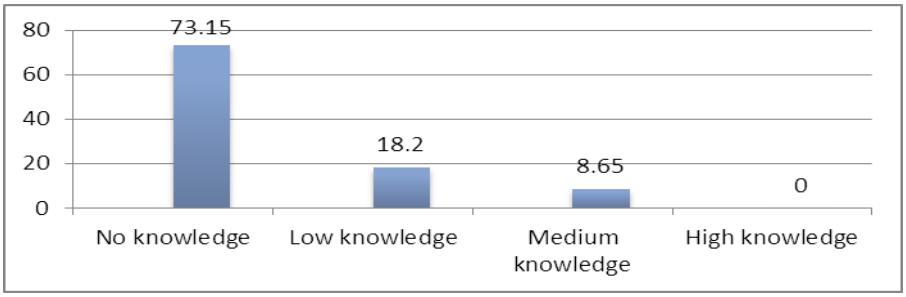

Figure 2: *The Distribution of Respondents Based on Knowledge of Arsenicosis*

3.5. Household Income and Arsenicosis Prevalence

The study was found that household income has negative relation to prevalence of arsenicosis problem in the study area. It was found who have higher income is more aware about arsenicosis problem. The study showed that the maximum number of arsenicosis patients (71%) belonged to low income group and 29% belong to middle class income group but none was found in high income group and all these patients were from rural areas of the country. Majority of all these patients was related with the traditional occupation of the country like cultivation (53%) in addition to lower level of educational background (81.5%). People who have low income, low educational background and individual who have been suffering from malnutrition are main exposure side of arsenicosis [7]. Health status of severe arsenicosis patients and loopholes of existing medical facilities in the study area.

3.6. Categorizations of the Arsenicosis Patients

Five category of arsenicosis pained had observed in the study area that's: leucomelanosis (initial stage), melanosis (1st stage), keratosis (2nd stage), hyperkeratosis, and skin cancer (3rd stage). In the study area highest 48.24% respondents were in initial stage (leucomelanosis), 21.18% were melanosis, 11.78% were keratosis, 3.5% were hyperkeratosis stages and 12.95% were not affected by arsenocosis.

Table 3: *Category of Diseases*

Category of Diseases	Percent (%) of Patient
Leucomelanosis (initial stage)	48.24
Melanosis (1st stage)	21.18
Keratosis (2nd stage)	11.78
Hyperkeratosis	5.5
Skin cancer (3rd stage)	10.9

This study correlates with the study of Guo et al. indicated that the prevalence of skin lesions like leucomelanosis and melanosis were highest prevalence in region of drank water from tube wells with higher concentration of inorganic [8].

3.7. Treatment Received from the Govt. Health Institution

Different types of treatment are available in the study area. The study represents that most of the patients (69.23%) received vitamins for arsenicosis treatment. Among rest of the patients, 7.65% patient got ointment for treatment and about 23.12% patient did not get any treatment for arsenicosis disease. The distribution of the respondents based on the treatment they received in the study area is shown in the following figure 3.

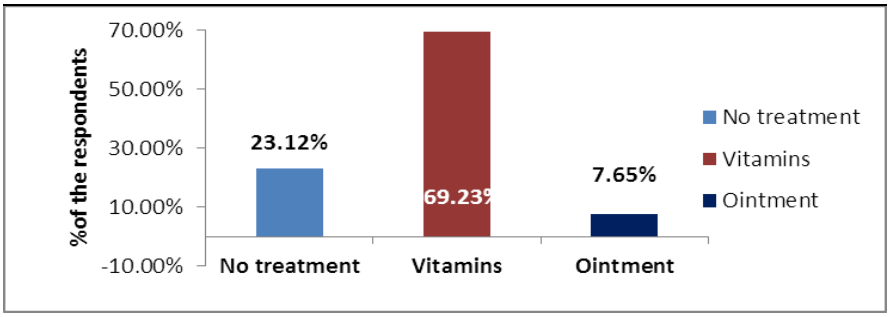

Figure 3: *The Distribution of Respondents Based on Medical Facilities*

3.8. Frequency of Treatment Received by the Patients

The study represents the times of receiving treatment of the respondents during last one year from the different medical facilities available in the study area. Most of the patients (49.61%) got treatment yearly for arsenicosis disease. Among rest of the respondents, 28.35% patients half yearly got treatment due to arsenicosis and about 15.68% and 6.36% patients got treatment quarterly, monthly respectively. The distribution of frequency of treatment received by the patients in the study area is shown in the following figure 4.

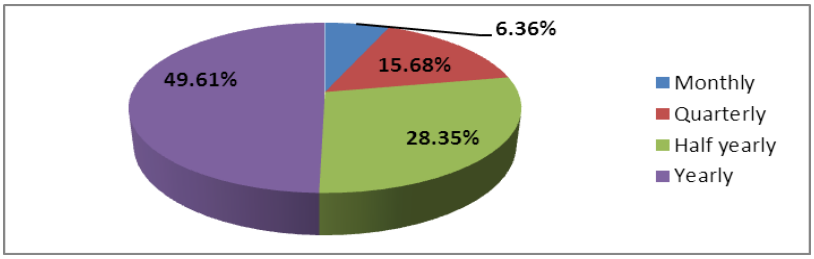

Figure 4*: The Distribution of Respondents Based on Frequency of Treatment*

3.9. Types of Support People Want to Cope With the Impact of Arsenicosis

Different types of support people want to cope with the impact. The study represents the types of recommendations of the respondents to get more improved treatment for arsenicosis disease. Most of the patients (45.58%) recommended free treatment and medicine can be provided regularly to get treatment. Among rest of the patients 20.80%, 14.65%, 6.85% and 12.12% patients recommended that more medical center should be established, loan can be provided, more arsenic safe water options can be established, regular physician visit should be established respectively.

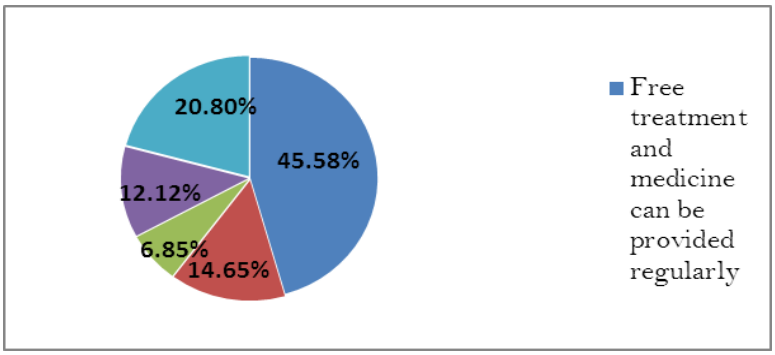

Figure 5: *Different Types of Support People Want in the Study Area*

Rahman et al., found a significant dose response relationship between arsenic exposure and diabetes mellitus among those suffering from keratoses in Dhaka, Bangladesh [6]. Deep tube-well is one of the other best alternatives for drinking water. According to record of British geological survey [12] out of 280 tube-wells only 2 are contaminated by arsenic above the limit. According to the study majority of arsenic patient are low income group and next is middle class (29%) group. Majority (53%) people of the patient engaged with cultivation in addition lower level of education background. So need to emphasis on supply on arsenic free drinking water and balance diet to the people by means of easy access to better nutrition facility. (Ratnaike R.N., 2003). The study results is similar with the results of Faruque et al. more than half (54%) regularly consumed well water with an as concentration ≥ 50 µg/L- above the acceptable government standard in Bangladesh due to lack of knowledge [13]. In West Bengal study also reveals that as safety level is not same in all the areas. This study correlates with the study of Guo et al. indicated that the prevalence of skin lesions like leucomelanosis and melanosis were highest prevalence in region of drank water from tube wells with higher concentration of inorganic arsenic [8].

This study reflects in the West Bengal study by Ahsan et al. reported that 21.6% of participants in the study had skin lesions of such as melanosis or blackspots [14]. These issues based on various studies are discussed below. Arsenic is not only a physical but also a social phenomenon [15]. Besides arsenic toxicity and arsenicosis diseases, arsenic poisoning creates extensive social implications for its victims and their families in affected areas. A number of socio-economic problems like social uncertainty, social; injustice, social isolation and problematic family issues are reported due to arsenicosis [14, 15]. Poor are the main victim of arsenicosis [14, 16, 17, 18], who have not easy access to alternative drinking water source and basic health facilities because of less income status. Long term arsenicosis problem could cause social problem and amplify the social problems [16]. Arsenic diseases have positive relation with income and poverty. Most of the arsenicosis patient could not take any treatment because of financial constraints. One of the study found that about 20-70% of the patients do not go for any treatment because of financial constraints in Bangladesh. The lack of treatment lessens the working efficiency of the poor and cause loss of job, barrier to aces new job and social rejection. Arsenic free water collection to family also matter of diminish the household income [15]. Social conflicts over contaminated water destroy the social harmony and network relationships [15, 18]. Arsenicosis victim wrongly treated and isolated from social and family relation, this creates social discrimination and hampers the social mobilization. Children of the arsenicosis patient being isolated from social and religious function, moreover they are not allowed to take baths in the village ponds [15] some unaffected people act like that the patient should stay in their home or leave their village in elsewhere [19]. There is lack of information to the rural people of Bangladesh about aresenicosis [15, 19, 20]. As a result some people think that the disease is an act of devil /impure air or the work of evil sprite. For this believe about 30-80% patients of arsenicosis patient do not take any treatment in Bangladesh [16].

4. Conclusion

In rural areas of Bangladesh, access to water is generally more problematic, more differentiated and less secure due to presence of arsenic in the drinking water source. For human consumption, water should be both safe and wholesome. Without ample safe drinking water, communities cannot be staying healthy. So, it is very urgent to ensure the enormous supply of safe water sources for the arsenic-prone areas. The current situation is that arsenic contamination is increasing in both severity and extent in the study area. Poor people are the most vulnerable to the effect of chronic arsenic diseases because of their lack of capacity to install arsenic free source of drinking water. In view of the increasing burden of arsenicosis- especially among the poor-the whole effort of arsenic mitigation should be considered as an essential part of the National Poverty Alleviation Strategy of Bangladesh. The present study will be helpful for the other researchers for doing research in arsenic related research in the study area and other organization.

The World Health Organization describes arsenic contamination problem as one of the world's primary environmental changes. Most of the population in the study area is continues to drink arsenic-laced water. Knowledge about the health hazards of arsenic contamination, availability of alternative arsenic free drinking water source abets them to face this devastating environmental challenge. To reduce the cumulative intake of arsenic by the population as a whole as rapidly as possibly the arsenic mitigation should be installed in the region. The short term and long term mitigation programs are

- The arsenic related problem should be declared a public health emergency to facilitate the rapid allocation of funding and prompt expansion of intervention
- Creation of awareness by health education
- All cases of arsenicosis should be identified; more research in the study area should be implemented
- An immediate interim source of arsenic-free water should be identified and the implementation of a long term solution should begin
- Chemicals to be used daily to remove arsenic from water
- Surface water should be used through filtration and chlorination
- Patients' progress should be monitored regularly by the health worker
- Rain water through rain water harvesting
- Surface water (pond/river) through pond sand filter

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Review Article | Open Access

Food Fortification to Combat Iron Deficiency Anaemia

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Abstract Among the various blood disorder anemia is a widespread health problem associated with an increased risk of morbidity and mortality, especially in pregnant women and young children. The major causes for anemia are both nutritional (vitamin and mineral deficiencies) and non-nutritional (infection and hemoglobinopathies). In particular, the major factors that contribute to the onset of anemia are iron deficiency and malaria. The present review focuses on the various intervention programmers for eradicating iron deficiency anaemia.
Keywords *Iron Deficiency Anemia, Iron Fortification, Elemental Iron, Hemoglobin*

1. Introduction

The reduced capacity of blood to deliver oxygen to body cells and tissue is called anemia (Provan, 1999). One of the major causes of anemia is Iron deficiency. This anemia can be defined as a defect in hemoglobin synthesis, resulting in red blood cells that are abnormally small (microcytic) and decreased amount of hemoglobin (hypochromic). Iron deficiency is the most common and widespread nutritional disorder in the world which is affecting a large number of children and women in developing countries (Figure 1). Malaria, HIV/AIDS, hookworm infestation, schistosomiasis, and other infections such as tuberculosis are particularly important factors contributing to the high prevalence of anemia in some areas (WHO Report, 2002). According to the third National Health and Nutrition Examination Survey (NHANES III) data, iron deficiency is defined by two or more abnormal measurements (serum ferritin, transferrin saturation and/or erythrocyte protoporphyrin). Iron deficiency anemia, a more severe stage of iron deficiency (defined as low hemoglobin in combination with iron deficiency), was found in 3.3 million females (Looker et al., 1997). Adolescence in India goes hand in hand with iron-deficiency anemia, medically known as IDA; according to the latest NFHS report, 56% of adolescent girls and 30% of adolescent boys are suffering from anemia. The National Family Health Survey (NFHS-3) conducted in 2005-06, presents the statistics that mark a growth in cases pertaining to anemia. Most of the anemic patients, especially women, suffer from mild to severe deficiency of iron. The hemoglobin count in most of the adolescent girls in India is less than the standard 12 g/deciliter, accepted worldwide (National Family Health Survey Report, 2008). The present review explain the

depth study on, need for iron fortification, common fortificants, foods available for fortification and success stories pertaining to it.

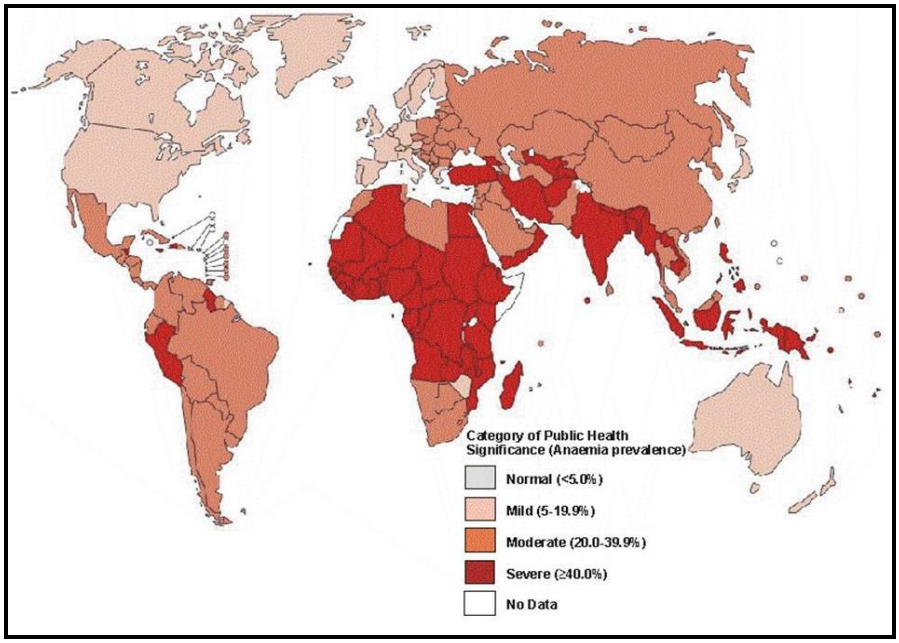

Figure 1: *Prevalence of Anemia on a Global Level*

Source: WHO, CDC. Worldwide prevalence of anaemia 1993-2005. WHO global database on anaemia. Geneva, World Health Organization, 2008.

2. Significance

Iron is essential to all cellular function in the body. It involves in varied cellular functions namely, energy metabolism, gene regulation, cell growth and differentiation, oxygen binding and transport, muscle oxygen use and storage, enzyme reactions, neurotransmitter synthesis, and protein synthesis (Beard et al., 2001). Potential consequences of iron deficiency, which occur in relation to its severity, are summarized in Table 1, while symptoms associated with anemia are listed in Table 2.

Table 1: *Potential Consequences of Iron Deficiency*

S. N.	Potential Consequences	S. N.	Potential Consequences
1.	Decreased maximum aerobic capacity	7.	Increased rates of infection
2.	Decreased athletic performance	8.	Impaired cognitive functioning and memory
3.	Lowered endurance	9.	Decreased school performance
4.	Decreased work capacity	10.	Compromised growth and development
5.	Impaired temperature regulation	11.	Increased lead and cadmium absorption
6.	Depressed immune function	12.	Increased risk of pregnancy complications, including prematurity and fetal growth retardation

Source: Provan, 1999

Table 2: *Symptoms Associated with Iron Deficiency Anemia*

S. N.	Symptoms	S. N.	Symptoms
1.	Fatigue	9.	Pallor
2.	Lethargy	10.	Flattened, brittle nails (spoon nail)
3.	Dizziness	11.	Angular stomatitis (cracks at mouth corners)
4.	Headaches	12.	Glossitis
5.	Shortness of breath	13.	Blue sclera (whites of eyes)
6.	Ringing in ears	14.	Pale conjunctivae
7.	Taste disturbances	15.	Pica (ice chewing)
8.	Restless leg syndrome		

Source: Provan, 1999

3. Etiology

Adolescents are vulnerable to iron deficiency because of increased iron requirements related to rapid growth (Wharton, 1999). About three fourths of adolescent females do not meet dietary iron requirements, compared to 17% of males (Centre for Disease Control and Prevention Report, 1998). Conditions which increase the risk for iron deficiency in adolescents are summarized in Table 3.

Table 3: *Risk Factors for Iron Deficiency*

S. N.	Inadequate Iron Intake / Absorption / Stores	S. N.	Inadequate Iron Intake / Absorption / Stores
1.	Vegetarian eating styles, especially vegan diets	7.	Meal skipping
2.	Macrobiotic diet	8.	Substance abuse
3.	Low intakes of meat, fish, poultry or iron fortified foods	9.	History of iron deficiency anemia
4.	Low intake of foods rich in ascorbic acid	10.	Recent immigrant from developing country
5.	Frequent dieting or restricted eating	11.	Special health care needs
6.	Chronic or significant weight loss		

Source: Provan, 1999

S. N.	Increased Iron Requirements/losses
1.	Heavy/lengthy menstrual periods
2.	Rapid growth
3.	Pregnancy (recent or current)

4. Intervention and Strategies

To maximize absorption, iron supplements should be taken with liquids such as fruit juices etc. Iron supplements should not be taken with milk, coffee, tea or phosphate-containing carbonated beverages such as soft drinks (Cook[a], 1999).

Dietary iron sources include meat, fish and poultry, lentils, dried beans, grain products, vegetables, dried fruit, and molasses (Table 4). The only approach would provide long term improvement of iron and cost effective is through food fortification using iron.

Table 4: *Dietary Factors that Enhance and Inhibit Iron Absorption*

Enhance	Inhibit
Meat	Phosphate
Fish	Calcium
Poultry	Tea (tannic acid)
Seafood	Coffee
Gastric Acid	Colas/Soft Drinks
Ascorbic Acid	Soy Protein
Malic Acid	High doses of Minerals
Citric Acid	Bran/Fiber

Source: Provan, 1999

5. Iron Fortificants

Some characteristics of commonly used iron compounds are shown in Table 5. They can be conveniently divided into four groups: (i) those that are freely water soluble; (ii) those that are poorly water soluble but soluble in dilute acids such as gastric juice; (iii) those that are water insoluble but poorly soluble in dilute acid; and (iv) protected iron compounds. The table gives guideline values for relative bioavailability in rat and man and a relative cost factor (Bothwell et al., 1992; Hurrell, 1985; Taylor et al., 1986).

Table 5: *Characteristics of Iron Sources Commonly Used to Fortify Food (Adapted from Hurrell 1985, 1992; Bothwell & Mcphail 1992)*

	Approximate Fe Content (%)	Average Relative Bioavailability		Approximate Relative Costa
			Rat	Man
Freely Water Soluble				
Ferrous Sulfate 7H2O	20	100	100	1.0
Dried Ferrous Sulfate	33	100	100	0.7
Ferrous Gluconate	12	97	89	5.1
Ferrous Lactate	19	—	106	4.1
Ferric Ammonium Citrate	18	107	—	2.1
Poorly Water Soluble				
/Soluble In Dilute Acid				
Ferrous Fumarate	33	95	100	1.3
Ferrous Succinate	35	119	92	4.1
Ferric Saccharate	10	92	74	5.2
Water-Insoluble				
/Poorly Soluble In Dilute Acid				
Ferric Orthophosphate	28	6–46	25–32	4.1
Ferric Ammonium Orthophosphate (EKA Nobel, Sweden)				
Ferric Pyrophosphate	25	45–58	21–74	2.3
Elemental Fe Powders:				
Electrolytic	98	4–48	5–100	0.5
Carbonyl	98	39–66	5–20	1.0
Reduced	97	24–54	13–148	0.2
Protected Compounds				
Nafe EDTA	14	—	28–416	6.0
Hemoglobin	0.34	—	100–700	—

A relative to ferrous sulfate $7H_2O$ = 1.0, for the same level of total iron

The bioavailability of iron for intake is depending upon the solubility in water. The water soluble iron compound is highly bioavailable compared to soluble in gastric juice as well as non soluble. The cost of the more recent or experimental compounds such as NaFeEDTA, ferric ammonium orthophosphate, and haemoglobin depend to some extent on the amounts ordered (Hallberg et al., 1989). In general, the freely water-soluble compounds are highly bioavailable in rodents and humans, as are compounds that are water insoluble but soluble in dilute acids.

5.1. Freely Water-Soluble Compounds

Ferrous sulphate is the least expensive compound and is widely used to fortify infant formulas and pasta and cereal flour that are stored for only short periods. Other possibilities are ferrous gluconate, ferrous lactate, and ferric ammonium citrate. (Forth et al., 1987) reported that there is no evidence that soluble ferric salts are absorbed to a lesser extent than soluble ferrous salts when iron is in an ionized form it is possible that ferric iron binds more strongly with inhibitors of absorption such as phytic acid and polyphenols.

5.2. Compounds Poorly Soluble in Dilute Acids

Compounds poorly soluble in dilute acids include ferric pyrophosphate, ferric orthophosphate, and ferric ammonium orthophosphate (Taylor et al., 1986; Patrick, 1985). They are the most often-used compounds in food fortification and their main advantage is that they cause no organoleptic problems. Their disadvantage is that they have a variable absorption because they do not readily dissolve in gastric juice.

5.3. Encapsulated Iron Compounds

Both ferrous sulphate and ferrous fumarate are available commercially in encapsulated form. Commonly, the coatings are partially hydrogenated oils, such as soybean and cottonseed, or ethyl cellulose. The coating has little influence on the Relative Bioavailability (RBV) as measured in rodent assays (Hurell, 1985) and can prevent fat oxidation changes during storage of cereals or in infant formulas fortified with the easily oxidizable longchain polyunsaturated fatty acids.

5.4. Characteristic of Good Vehicle for Fortification

The choice of food matrix and iron source should have optimal combination for effective biological impact. The best iron compounds (ferrous fumarate/sulphate, bisglycinate or NaEDTA) with carrier that have high levels of inhibitors will not be effective. For effective food fortification, that the fortified food is consumed by the target population is low in cost and has good organoleptic properties. Failure of fortification efforts to prevent iron deficiency can be explained in most cases by lack of compliance with these criteria. The process of selecting the best food vehicle and iron source may appear simple but is actually a complex process that requires evaluation at every step. The physical properties of iron compound reacting with food carrier is a concern for fortification particularly color and flavor.

6. Major Vehicles for Iron Fortification

6.1. Cereals

Cereals are the most widely used vehicles for iron fortification. (Baurenfiend et al., 1990). The contribution of fortified iron to iron intake is highest in the United States, where it accounts for 20–25% of total iron intake (Subar, 1988; Lachance, 1989). The contribution of fortified iron to iron intake in the United Kingdom is much lower; around 6% (Hurrell et al., 1996). Whole grain rice is fortified by coating, infusing, or by using extruded grain analogues. Other commonly fortified foods are breakfast

cereals and infant cereals. While fortification of wheat flour, sugar and salt with iron is a common strategy in industrialized countries, fortification of millet flours with the same element has gained little attention (Subbulakshmi et al., 1999).

6.2. Salt

Iodine-fortified salt has successfully used to eradicate iodine deficiency in many countries (Dunn et al*.,* 1986). However, iron fortification of salt poses many technical problems. Moreover, an efficient production and distribution system is important. Salt that contains fewer impurities would undoubtedly be easier to fortify, but the extra cost for purification passed to the consumer is always a major consideration in developing countries. Technical constraints do exist with salt fortification, but it is possible to overcome these limitations. In addition, there is always the possibility that the iron-fortified salt will cause unacceptable color reactions if added to vegetables in a meal.

6.3. Sugar

Sugar is an alternative vehicle for iron fortification particularly in regions of the world where it has been produced enormously is produced, such as the Caribbean and Central America. However, in other developing countries, the consumption of refined sugar is more common in major socioeconomic segments of the population (Cook et al., 1983).

6.4. Milk

Infant formulas are usually milk based with added vegetable oils, minerals, and vitamins. Iron is almost always added as ferrous sulphate from 5 to 12 mg per liter (Lynch, 1990). Its absorption can be improved considerably by the addition vitamin C (Stekel, 1986). The inhibitors which limit the availability of iron in the milk are calcium (Hallberg et al., 1991) and the milk protein casein (Hurrell et al., 1989). Though vitamin C increases the availability of ferrous sulphate it is difficult to add vitamin C to fluid milk since it degrade milk rapidly to diketogluconic acid leading to changes in flavor (Hegenauer et al., 1979).

6.5. Condiments

Condiments that are traditionally used in developing countries, such as monosodium glutamate, fish sauce, curry powder, and bouillon cubes, could be useful fortification vehicles.

6.6. Coffee

In some countries coffee is consumed by most adults as well as some children, and it is technically and economically feasible to fortify coffee with iron. Johnson and Evans 1977 reported the use of ferrous fumarate in roasted and ground coffee, in which one cup (200 mL) provided 1 mg added iron. The addition of iron to soluble coffee is also relatively easy. (Klug et al., 1973) reported that the addition of a range of soluble ferrous and ferric compounds was possible. Flavor and color changes, however, are a potential problem, and coffee, like tea and cocoa, contains phenolic compounds that strongly inhibit iron absorption.

7. Success Stories of Iron Fortification

Experiences from the above trials conducted, should help to accelerate the implementation of effective large-scale iron fortification programs. They underscore the fact that when a carefully selected food vehicle and a relatively bioavailable iron compound are combined and consumed by at-

risk groups under supervised or normal market conditions, there can be a measurable and important improvement in iron status associated with the introduction of the fortified foods.

These included the need for appropriate quality control at mills; nutrient losses due to cooking in excess water; and lack of information on nutrient loss during storage. Decades of research on rice enrichment and fortification practices have provided a better understanding of the technology needed; however, some technical problems remain. With the exception of vitamin A, the cost of the added nutrients to cereal grains is negligible. Ranges from 1.5 cents per person per year for added iron to 29 cents per person per year for added vitamin A have been reported (Lotfi et al., 1996). Commercial vitamin mineral premixes can reduce the quality control costs by providing uniform nutrient levels. The capital costs of launching a food enrichment/fortification program, however, must be balanced against the cost of not implementing a program which may result in public health problems, increased medical costs, and decreased productivity due to resulting deficiencies. United States Agency for International Development and Opportunities for Micronutrient Interventions (USAID/OMNI) has investigated the cost-effectiveness of various strategies to improve micronutrient status, including food fortification programs. Program planners can learn from the decades of experience in rice fortification technology. Applying known rice fortification technology in rice consuming countries where deficiencies are common provides an opportunity to reduce the economic and social burdens that are placed on the population due to micronutrient deficiencies. The benefits to the producer and the miller of adding value to 1 rice by improving its nutritional quality needs to be determined to promote food fortification programs.

8. Conclusion

Fortification requires careful selection of vehicle and then adopting a proper technique to fortify the raw material, and then proper amount of consumption of the fortified material.

Considerations

- Fortification of staple/complementary foods and condiments can be successfully implemented with proper attention to the selection of fortificants.
- Product research and development, operational research, program planning, communication strategy, advocacy, private/public partnerships and legislation are vital for effectiveness.
- Operational research on how to overcome practical barriers for successful implementation of fortification, from which practical lessons can be learned, should be undertaken.
- Fortification is one of several approaches to achieve this goal and, specifically, to combat iron deficiency. However, fortification should always be considered as one component of an integrated strategy.

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Research Article | Open Access

Globalization of Clinical Trials- A Review of Underlying Ethical and Scientific Considerations Involving Human Subjects in India

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Abstract The conduct of clinical research involving the participation of human beings embroils a variety of ethical issues like dignity, liberty, autonomy, privacy and bodily integrity. The ethical conduct of a clinical trial just not only includes a signature on the informed consent form by the concerned participant but protecting the dignity, rights, interests, and safety of research subjects must continue throughout the duration of the study. Pharmaceutical industries are legally and ethically bound to protect human participants involved in clinical research. This article reviews and describes the scientific and ethical aspects of clinical trials and necessary regulatory mechanism to protect the rights, dignity, and privacy of human subjects: the institutional review board, the Ethical committee, the sponsor, the informed consent process and the investigator in developing countries like India. This article also reviews some of the important issues like informed consent, payment for participation in a clinical trial, and defining standard of care in critically ill patients.
Keywords *Ethical Committee, Pharmaceutical Industries*

1. Introduction

Globalization is the process of interchange of different views, products, ideas, services and culture across the boundaries resulting in international integration. Globalization has wide impacts on societies across the world. In a definition of Globalization given by Lee “all the spheres of human interaction including social, political, economic, environmental eroding the boundaries of all kinds come under globalization” [8].

Globalization on one hand has resulted in greater economic growth, prosperity, cost savings and short timeline for clinical testing, but on the other hand critics point to the exploitation of subjects, risk to their health and emergence of economic disparities particularly when clinical trials are conducted in low- and middle- income countries. Globalization has proved to be a boon for biomedical and pharmaceutical companies in terms of their business.

In 2009 Glickman *et al* in his study "Ethical and scientific implications of globalization of clinical research" raised important questions about the economical and ethical issues of clinical research. Findings of the study show that approximately one third of the trials (157 of 509) are conducted outside United States and a majority of study sites (13521 of 24206) are outside United States in developing countries. In the report developing country trials are labeled as scientifically questionable and morally inappropriate [12]. The study concluded that genetic and other population differences could render results that did not apply to the target population [12]. The report also raised concerns that money was paid in recruiting poor volunteers. He explained reasons for this dramatic shift that pharmaceutical companies realize cost savings and shorten timeline and less regulatory barriers in developing countries for clinical testing [12].

In a study Ethical issues in tuberculosis vaccine trials conducted in 2000 by Dixie E. Snider certain ethical issues like generic issues against tuberculosis in involving human subjects in developing countries were raised [3]. The results of study show that there was exploitation of trial subjects for testing interventions in developing countries [3].

An article in New England Journal of Medicine in 19 February says that the twenty largest U.S. -based pharmaceutical industries conduct about one third of their phase III clinical trials outside the country and a majority of their study sites also are outside United States. Article says that two decades ago, nearly all of these clinical trials were done in the U.S. The number of trials in developing countries has grown 8% a year since 1997, according to Food and Drug Administration data [7].

In a study in 2010 "Clinical Research ethics in developing countries: challenges and the way forward" Dr. Ballari Brahmachari and Dr. Arun Bhatt concluded that the trend of globalization in clinical research is increasing with more and more sponsors in economically advanced countries outsourcing trials to developing nations. According to this study the reasons behind this is less cost in conducting trials and a large pool of patients for any disease ensuring rapid recruitment and lesser timelines for completing clinical trials [18].

According to a survey done by Journal of medical ethics in February 2004 less than six out of 10 trial protocols are reviewed by an ethical committee. In China only one out of 10 trial protocols are reviewed [7].

Biomedical research is conducted for collecting and analyzing data from which conclusions are drawn that help in improving the care of currently unknown beneficiaries in the future. Human participants are the important sources of data in this regard. This phenomenon raises important questions about the moral, social, economic and ethical issues of clinical research. Recently in conducting clinical trials more emphasis is laid on monitoring welfare of participating subjects during the conduct of research. Just taking an informed consent form does not account for the moral, social and ethical concerns in conducting clinical trials. Safety, rights and interests of the human subjects for clinical trials should be ensured and continued throughout the duration of study. This article describes and defines the underlying reasons for globalization of clinical trials, bring out the important moral, ethical and behavioral concerns associated with the globalization of clinical research, the monitoring regulatory bodies to ensure the adequate protection of the dignity, rights and welfare of participating human subjects and review of responsibilities of the regulatory bodies: the institutional review board, the data monitoring committee, the sponsor, and the investigator. This article also reviews and proposes the important steps for compliance and harmonization of globalization of clinical trials.

2. Background of Globalization of Clinical Trials

In the process of clinical trials safety and effectiveness of a new drug is tested. When a new drug is discovered and developed by a pharmaceutical company, extensive pre-clinical trials are conducted

prior to testing the drug on people. This pre-clinical process of development of drug ensures the safety of drug for human beings, the starting dose of drug for human clinical trials, and the reaction of new drug on the human body. Once pharmaceutical companies gather enough information regarding the drug these methods can be applied to determine the affectivity of a treatment. As many multinational companies from developed countries have outsourced tasks like computer support and customer service to other countries, pharmaceutical companies have followed the same by outsourcing clinical trials to developing countries like India in addition to the sites in developed countries. India is considered to be a favorable site for conduct of clinical trials as there is large, diverse and untreated population and a pool of patients with both acute and chronic diseases. As the scope of outsourcing clinical trials to developing countries in biomedical research is increasing, ethical and social questions regarding adequate protection of the dignity, rights and welfare of participating human subjects have re-emerged. Recently ethical issues in clinical research are gaining importance because of the concern that research conducted by pharmaceutical companies from developed countries in developing countries like India that is flooded with diseases of almost all types is imposing ethically and morally inappropriate burdens on the host country and the participants in the research trials. This has caused the regularity authorities to realize the importance of ethical issues to ensure that adequate ethical and economical protection is provided to all persons who participate in international clinical trials.

Since 2002, 15% annual growth has been observed in the number of active Food and Drug Administration (FDA) – regulated investigators based outside the United States, whereas the number of U.S. - based investigators has decreased by 5.5% [12]. This trend suggests that clinical research industry is undergoing the same process of globalization as other industries by outsourcing clinical trials to poor countries [9]. According to Tuff's study in 1997, about 86 percent of F.D.A. - regulated investigators were based in the United States. By 2007, the number of FDA regulated trials conducted in United States decreased to 54%. Pharmaceutical companies from developed countries are looking for developing countries like India because it is often less expensive to conduct clinical trials outside the developed countries and it is easier to find a large group of subjects who had never been treated with medications [9].

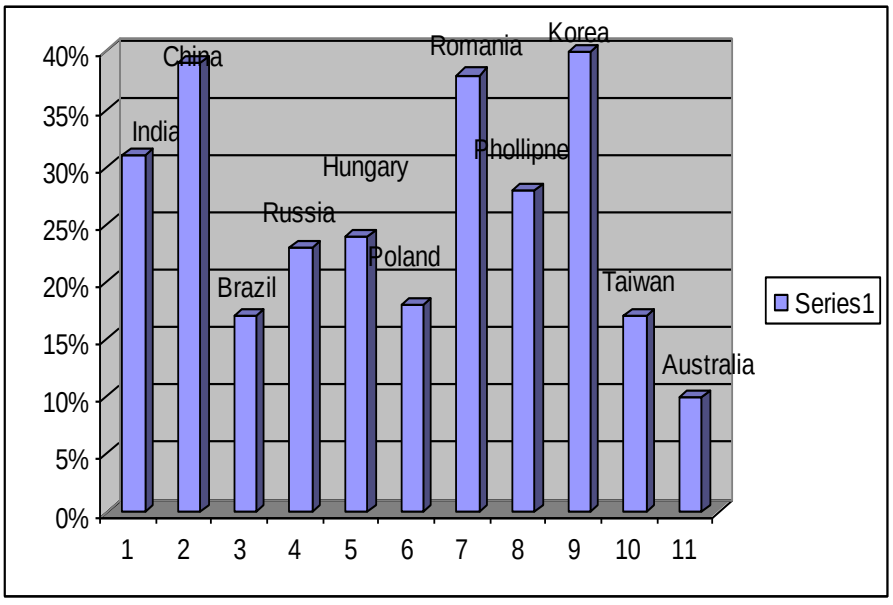

Figure 1: *Clinical Trial Market- Comparative Analysis of Trials among Different Countries According to Data in www.clinicaltrials.gov*

3. Reasons for Globalization of Clinical Trials

What are the reasons behind this globalization and dramatic shift in the location of clinical trials? Why India is becoming a preferable site for conduct of clinical trials by pharmaceutical companies from developed countries? There are many underlying reasons responsible for this.

3.1. Access to Subjects

According to a report by Department of Health and Human Services programs sites in India allow pharmaceutical companies from developed countries to recruit subjects quickly and, therefore, bring their drugs to market faster. Subject's recruitment is reported to occur more quickly in India than in developed countries.

3.2. Economical Benefit

Pharmaceutical and biomedical companies gain substantial cost benefits by conducting trials in India**.**

3.3. Genetically Diverse Population

India is a favorable site for conduction of clinical trials because of its genetically diverse population who have not been exposed to many medications but have pool of diseases, ranging from tropical infections to degenerative disorders.

3.4. Low Infrastructure Cost and Cheap Labor

Almost all Indian doctors speak English, and many have acquired postgraduate qualifications abroad, primarily in developed countries. Besides this cheap labor and low infrastructure costs, which can reduce expenditures for clinical trials by approximately 60 percent, is available in India [18].

3.5. Bureaucratic Regulatory Procedure in Developed Countries

Furthermore, the Drugs Controller General of India (DCGI) — the equivalent of the U.S. Food and Drug Administration (FDA) — is understaffed and lacks the expertise to evaluate protocols. Currently, the technical staff consists of just three pharmacists, including the controller, and just one medically qualified doctor. The reason for conducting clinical trials in developing countries is increasingly bureaucratic and expensive regulatory environment in developed countries. In developed countries the laws and regulations governing the clinical research trials have become more and more complicated which in turn place a greater burden on clinical research investigators for documentation, training and devices on a global scale.

4. Regulatory Mechanism for Conduct of Clinical Trials in India

4.1. Regulatory Procedures

The Central Regulatory agency known as the DRUGS CONTROLLER GENERAL (INDIA) or the DCGI is responsible for all procedures related to new drugs including clinical trials in India. All clinical trial applications are submitted to the DCGI office for approval. The documents required as part of the clinical trial application are detailed in Form 44 under Schedule Y of the Drugs and Cosmetic Act. Permission to conduct trials is granted in approximately 3 months from the time of submission. The approval process takes longer if the DCGI's office decides to refer the application for expert feedback to agencies such as the Indian Council of Medical Research (ICMR). If the drug falls under the category of "genetically engineered" or "biologics" then the application is passed through to the

Department of Biotechnology (DBT) and is reviewed by the Genetic Engineering Approval Committee (GEAC). This approval process usually take anywhere between 5 - 6 months. Along with the clinical trial application, an application for import license is made by completing Form 12 of Schedule Y. The application should accurately quantify the drugs imported accompanied with appropriate justifications for the quantities imported. An import license number is issued about 2 weeks after the clinical trial approval is provided. This import license number should appear on all the individual subject drug supplies [2].

If biological samples need to be shipped out of India, an application for export needs to be made to the Director General of Foreign Trade (DGFT).

The Central Drugs Standard Control Organization first issued the Indian Good Clinical Practice (GCP) guidelines in year 2001. These guidelines were subsequently amended and made the law in the year 2005.

Sponsors need to be aware of each of these differences and ensure adherence to Indian guidelines at all times.

4.2. Ethics Committees

In India most of the hospitals have institutional Ethics Committees for review of clinical trials. These committees are formed as per the guidelines issued by GCP. At a minimum, the documents submitted to committee are Protocol and Investigator Brochure including all amendments, informed consent forms along with translations as well as details of payment or compensation to subjects, if any. Approval is received in maximum of six to eight weeks following submissions. Most Ethics Committees usually charge a fee of approximately 200 US$ or 170 Euros. Some Ethics Committees chose to provide conditional approval until regulatory approval is received. Once regulatory approval is received, a full approval is provided in a matter of few days [2].

In a reflection of the increasing number of clinical trials being performed in India, several Independent Ethics Committees have begun functioning in the last couple of years. Sponsors usually approach the Independent Ethics Committees when they need to work with potential investigators with a private practice that not attached to a hospital or institution. However, in reality, ethical committees work very differently and rarely follow the GCP guidelines. There is no interest in their impact either. Just a complacent smugness about clinical research opportunities, almost like they are simply commercial ventures on the lines of call centers [2].

The second question relates to social ecology and the genetic makeup of trial populations. Geographically distinct populations can have different genetic profiles, and these differences have been shown to be related to the safety and effectiveness of drugs and even medical devices. Hospital and clinic infrastructure, treatment choices, and quality of care vary widely from country to country. Proper physician training is essential before providing the patients access to medications.

4.3. Informed Consent Process

Issue of informed consent is very important as far as India is concerned. Illiteracy as well as the possibly blind acceptance of the doctor’s advice amongst semi - urban and rural populations naturally rises sponsors’ concerns about how truly “informed” the informed consent process is in India. A recent issue of the journal CR Focus published by the Institute of Clinical Research carried an article on this very topic. The authors who are auditors and have audited studies all across the globe concluded that that the informed consent process carried out in India is probably as good or bad as anywhere else in the world [2].

Population of India is large and people speak different languages here. So informed consent document should be translated into the regional languages of the subjects. If the issue is of illiteracy any close relative of the subject can be brought for the process to serve as representative who is legally accepted for the informed consent process and side by side thumbprint impression of the subject can be obtained on the consent form.

As per the Indian guidelines, the subject can refuse to allow his biological material to be stored and used for future evaluations. The Indian GCP guidelines clearly define the content and format of the Informed Consent document and must be adapted for all clinical trials being performed in India.

4.4. Investigators

After USA India has good number of qualified doctors who are GCP trained. Since India is becoming a hub for clinical trials, the number of GCP trained doctors is expected to be doubled in coming two years. Doctors in India possess good communication skills, are well versed in English and are quite familiar with the trends of western medicine practice. According to my opinion sponsors for clinical trials and CROs need to train investigators lacking awareness about GCP guidelines for better results before starting any trial. Investigators participate in clinical trials as they get good opportunities in terms of being associated with international organizations apart from financial reasons. They can also provide free treatment to their patients also and get good grant from sponsors and learn latest techniques of investigation and treatment. All these factors push them towards participation in clinical trials.

5. Ethical and Scientific Considerations of Globalization of Clinical Trials in India

There are obvious reasons for conducting clinical trials in India. But there are certain important ethical and scientific issues raised by globalization of clinical trials [16, 14].

The most important ethical issues raised by the use of human participants in research are beneficence (doing good), non-malfeasance (preventing or mitigating harm), fidelity and trust within the fiduciary investigator/participant relationship, personal dignity, and autonomy related to privacy of information and informed, voluntary, competent decision making [1].

In India regulatory body which monitors the quality of clinical trial data and the safety of drugs and devices is the Drugs Controller General of India (DCGI), they have limited information regarding research conducted outside their jurisdictions or countries, including the sites, investigators, and participants and the quality of trial data [12, 10, 17].

Recently practice of unethical and illegal clinical trials has been observed in India which has attracted coverage by media also [11]. Many unethical cases have been observed like in 2002 two new chemicals M4 and G4N were used for the patients suffering from oral cancer at a regional cancer in Kerala which is run by the government. All those trials were done without any regulatory approval [11]. Also in the year 2003 an anticancer drug named Letrozole was used in illiterate women of West Bengal to test for ovulation which was again unethical [11].

Transparency in conducting trials in India is the main concern as far as ethical issues are concerned. The International Committee of Medical Journal Editors has issued guidelines for investigators with regard to participation in study design, access to data, and control over the publication of results [12, 6]. Protection of publication rights for investigators is necessary to the transparency and integrity of research, yet it is an ongoing area of contention for industry sponsors. What should be the criteria for enrolling human subjects in clinical trials? Pharmaceutical industries conducting clinical research

should be responsive to the health needs and priorities of the communities in which the research is conducted.

Table 1: *Issues, Obstacles and Recommendations for Globalization of Clinical Trials in India*

Issue	Obstacles	Recommendations
Transparency of clinical trials in India	Access to clinical data about the trials of the drugs which are not successful is usually not published and publicized	Information about failures of the trials should also be put in a publicly searchable database.
Informed consent	Sometimes surrogate or waved consent is obtained leaving patients unaware that they are in clinical trials particularly in critically ill patients.	An ethically valid informed consent consisting of four key components: disclosure, understanding, voluntaries, and competences should be mandatory before conducting clinical trials on human subjects. Even if in cases requiring exemption from informed consent like in critically ill patients or if family members are not available community consultation, public notification, and independent data and safety monitoring should be done.
Confidentiality	Sharing information from DNA sequencing, databanks and public health measures is essential for developments of new drugs	Researcher's goals against requiring essential information should be thoroughly balanced against the risk of harm which may occur due to disclosure of important information in an unauthorized way. A strict vigilance is needed in order to win the trust of the public which is an essential element in pursuit of knowledge to win the confidence of the research participants.
Exploitation of research participants	Recent studies have showed that some pharmaceutical companies offer financial inducements to the illiterate blue collared workers more per month to participate in a trial than they ears at their jobs and entice the subjects by providing medications. There is no protocol of continuation to supply the studied medicines free of charge or at affordable charges after completion of trial if found beneficial.	After the trial participants should have access to medicines after the trial if found to be effective they should not only be treated either free of cost or at discounted prices. A protocol should be made regarding supply of medicines after the trial at affordable charges for the participants.
Regulatory bodies	Regularity bodies like Drugs Controller General of India DGCI are understaffed and lack the expertise to evaluate protocols. Currently the technical staff consists of three pharmacists including the controller and not one medically qualified doctor.	The regulatory bodies should be properly staffed and increase qualified manpower and bringing in more academic expertise to discuss necessary improvement strategies for conduction of clinical trials in India. The required authority can be delegated to the lower ranks, which would shorten the approval timelines for clinical trials. The regulatory bodies recognize the need to frame guidelines and regulatory approval processes at par with international standards.

Compensation for participation	Most of the times participants enrolling in clinical trials are not reasonably financially compensated for their participation but simply benefit from free treatment, including doctor consultations, transportation, etc. Participation in clinical trials carries some risk and injury may occur during certain procedures.	Participants should not only receive fair and reasonable monetary compensation for the time and effort they devote for the clinical trials but should also be compensated for any injury if occur during clinical trial. A proper list of approximate monetary compensations for a variety of frequently performed clinical activities should be framed by the regularity bodies.
Review process	Pharma companies, clinical research organizations and investigators demand immediate reviews from institutional review boards which result in unqualified approval often made without extensive deliberation and scientific insight.	Centralized IRBs should receive more feedback about developments in multisided trials, and a “data safety monitoring board” should review those trials. IRBs should be informed of FDA actions against investigators and notified of prior protocol reviews conducted on the same protocol by other IRBs. They should increase their awareness of research conduct at the sites they review. Educational programs should be instituted for IRB members, along with continuing research ethics programs for participating physicians.
Documentation and communication	Translation of clinical trial documents requires a high level of precision and accuracy compared to other types of documents. Urbanization trends in many developing and emerging countries often result in diverse patient populations with wide and considerable linguistic and cultural differences from area to area and sometimes within a given area in India. Lack of education among research participants in India is thus the biggest challenge.	Documents submitted to the regulatory authorities must be translated into the official language of host country. The documents should be legible, clear, complete, clearly labeled, and accurate and filed in the pre-determined timeframe without any discrepancies. Documentation should be divided into three parts - before list, during list and after list. Before List consists of regulatory and ethics committee approvals, ICFs, subject information sheets, investigator brochures, finance and insurance agreements, investigational product specific guidelines, protocol, randomization lists, and pre-trial monitoring reports. Documentation ‘during’ the trial includes amendments, updates and approvals for them, ICFs and CRFs – completed, signed and dated. Adverse events (AE) reports and notifications, site staff logs, reports of monitoring visits, source documents are also filed. The ‘after’ list reads – audit certificates, final reports to be submitted to the regulatory authorities, trial close out monitoring report, clinical trial materials accountability records, decoding documentation and investigational product destruction records. All these documents are filed in the trial master file and the site master file and they serve to demonstrate compliance with GCP and regulatory norms. Documentation should comply with the necessary regulations and guidelines and their location and date of filing must be easily identifiable. Good documentation should ensure to fully reconstruct the trial even after it has been completed.

Post trial access	There is no regulatory requirement for provision of medications after completion of trial. Sometimes medicines are not available at all or are too expensive for the patients to afford.	As per WMA declaration of Helinskiy, it is necessary during the study planning process to identify post-trial access by study participants to prophylactic, diagnostic and therapeutic procedures identified as beneficial in the study or access to other appropriate care. Post-trial access arrangements or other care must be described in the study protocol so the ethical review committee may consider such arrangements during its review Patients who take on the inconvenience and potential risks of a medical research study should have access to the best proven prophylactic, diagnostic and therapeutic methods that result from the study.
Professional competence	In many cases the investigators involved in clinical trials are not sufficiently well trained to cope with advanced multidisciplinary environment. Training lacks minimum set of common requirements which undermines the scientific validity of trials.	Investigators involved in clinical trials should be thoroughly trained to cope with recent advances. This includes skill in counseling, informing and communicating adequately, participating in the decision-making process with respect to clinical trials.
Communication	There is no direct communication between industry and DCGI's office. So some applications are queried outright without checking the information.	An environment for effective interaction between regulators, industry and academia should be created. Regular meetings should be organized to discuss different issues.

6. Discussion and Conclusion

Although globalization of clinical trials has received considerable attention but there are certain ethical and scientific concerns that need to be taken care of as little attention has been devoted in quantifying the dimensions of such controversies. In this paper we have tried to bring such issues to the surface reflecting why India is considered to be a favorable destination for pharmaceutical companies for conducting clinical trials. There are two types of factors influencing participation of human subjects in clinical trials in India- one is the factors favoring participation and other is the factors restricting the participation. Factors favoring participation includes extra source of income, personal health benefits and motivation to participation in research for welfare of humanity.

In a developing country like India where poverty is rampant, participating in trials that offer monetary incentives is an extra source of income. Even when the trial does not offer any monetary compensation, the free care and treatment serves as a strong attraction for patients who otherwise cannot afford the cost of treatment. Given the influence of an incentive, its ability to distort potential participants' judgment towards trial participation is significant [16]. Rapid enrolment of participants in clinical trials, huge and racially diverse population ensuring generalizability of results also makes India an attractive destination for clinical trials.

Clinical testing in developing countries like India is also attractive to pharmaceutical and device companies because it can help them overcome regulatory barriers for drug approval in these countries in which the population size alone offers the promise of expanding markets [13].

Factors restricting participation include loss of confidentiality, concern about safety of drugs in trials and mistrust on pharmaceutical industries conducting trials.

Recent studies have showed that some pharmaceutical companies offer financial inducements to the illiterate blue collared workers more per month to participate in a trial than they ears at their jobs and entice the subjects by providing medications. There is no protocol of continuation to supply the studied medicines free of charge or at affordable charges after completion of trial if found beneficial.

Sometimes participants enrolling in clinical trials are not reasonably financially compensated for their participation but simply benefit from free treatment, including doctors' consultations, transportation, etc. Participation in clinical trials carries some risk and injury may occur during certain procedures.

In our opinion various prerequisites should be considered so as to have a positive effect of globalization on health of participants in clinical trials and to address ethical concerns raised by globalization of health (Table-1).

A careful effort to streamline regulations governing clinical trials could reduce redundancy in the system while ensuring ethical conduct. Improved research efficiency would decrease the differential costs of research among countries and increase the likelihood that trials are initiated in the countries where the drugs being tested will be sold. Greater use of centralized institutional review boards, standard terms for research contracts, and the development of streamlined best practices to reduce unnecessary work for investigators and medical institutions are needed [5, 4].

It is the complete responsibility of the research organizations and pharmaceutical industry sponsors that all the trials should meet ethical guidelines so as to face the challenges posed by globalization [12].

Documentation should comply with the necessary regulations and guidelines and their location and date of filing must be easily identifiable. Good documentation should ensure to fully reconstruct the trial even after it has been completed.

Participants should not only receive fair and reasonable monetary compensation for the time and effort they devote for the clinical trials but should also be compensated for any injury if occur during clinical trial.

A proper list of approximate monetary compensations for a variety of frequently performed clinical activities should be framed by the regularity bodies.

Investigators and sponsors involved in clinical trials should make best possible efforts to maintain confidentiality and access to medicines that have been proven effective for the participants.

Research proposals for clinical trial conduction submitted to ethics review committees should underline how new interventions that if proved to be effective from the research will become available in host country after the completion of trial. Pre-research negotiations among sponsors, host country officials, and other appropriate parties should be described thoroughly how such interventions will be made available.

Clinical trial participants take risks and accept inconveniences to promote the advancement of medicine. Hence to avoid exploitation and to maintain a good relationship between the investigators and participants, they deserve benefits in return for their contribution. Therefore, providing them successfully tested drugs is a good way of avoiding exploitation. NBAC also concludes that at the end of a clinical trial that results in an effective intervention, research participants should be provided with this intervention. In addition, NBAC also maintains that before initiating a research project, researchers or sponsors should consider how they might make benefits, if any, available to others in

the host country, with the understanding that appropriate host country decision makers must be meaningful and essential participants in making such arrangements.

Thorough review and proper assessment of different regulations governing clinical trials in India is required so as to get international acclaim in the field of clinical trials [19]. All the regulating factors need to be streamlined. Government should increase spending on clinical trials so that ethical issues can be dealt easily. Proper training should be given to the investigators in India regarding ethical and scientific considerations as well as design and process of clinical trials.

Transparency of clinical trials is the most important issue in India. Information about failures of the trials should also be put in a publicly searchable database.

Accordingly, provisions for the publication of all clinical trial data and protection of publication rights for investigators should be preserved, independent of sponsorship [12]. We suggest that to ensure the ethical and scientific integrity of clinical research globally and to promote harmonization of international research it is first necessary to overcome the barriers and provide thorough and complete information about the benefits and risks of new drugs in a publicly searchable database.

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