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HIV Infection and Nutrition: the Indian scenario

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During the first half of the last century India and other developing countries had struggled to combat the vicious cycle of under-nutrition predisposing people to infections and infections aggravating under-nutrition; mortality rates were high due to poor access to both health care and nutrition care. Later, the advent of antibiotics and improved access to health care reduced the impact of infections on nutritional status and mortality. Nutrition and health interventions resulted in some improvement in nutritional status especially in children. In the seventies there was optimism that soon the nutrition-infection vicious cycle could be broken. In the eighties the emergence of the Acquired Immuno-Deficiency Syndrome (AIDS) epidemic characterized by severe wasting, high morbidity due to a variety of opportunistic infections, and death within a short period after diagnosis shattered this hope. The high case fatality rates within one year after detection of the disease created panic among the population and serious concern among the health professionals. Combating under-nutrition, infection and mortality came back to the centre stage of health sector priorities.

The global research community responded vigorously to the AIDS pandemic; in 1984 Human Immunodeficiency Virus (HIV) was identified as the causative organism and serological tests for detection of HIV antibodies were developed in 1985. A global network of sero-surveillance centres for HIV infection and surveillance of AIDS cases was established to document the modes of transmission and determine the course and outcome of HIV infection. With the development of anti-retroviral drugs intervention programmes to combat HIV infection were initiated in all countries. As a result there has been a global decline in new infections and mortality associated with HIV infection in the last fifteen years. The vigour with which the global community combated the new pandemic over three decades made it possible for the world to achieve the Millennium Development Goals (MDG) target of halting the increase in HIV incidence by 2015. Encouraged by this achievement, the global community has now set the Sustainable Development Goals (SDG) target of ending the epidemic of HIV infection by 2030.

In the 1980s the Indian health system already had vast experience in combating millennia-old endemic infections and under-nutrition but always faced the disadvantage of having to cope with the large size of the affected populations. For reasons as yet not clear, HIV infection reached India and Asia late, granting the Indian health system an opportunity to show their mettle in tackling an epidemic detected in the early stage. India evolved and implemented the

National AIDS Control Programme (NACP) using the priority interventions identified on the basis of the national sero-surveillance; the country succeeded in providing the needed health care to HIV-infected persons without any disruption of the other health programmes. The HIV epidemic did not have any impact on the rate of decline of under-nutrition and mortality rates in the country. Within a decade after initiation of the NACP, there was a decline in the rate of new HIV infections; the country achieved the target set for HIV infection under the MDGs. India hopes to achieve the SDG targets by 2030. This manuscript will review the evolution of AIDS pandemic: global and Indian, and impact of health and nutritional interventions for persons living with HIV infection/AIDS (PLHA).

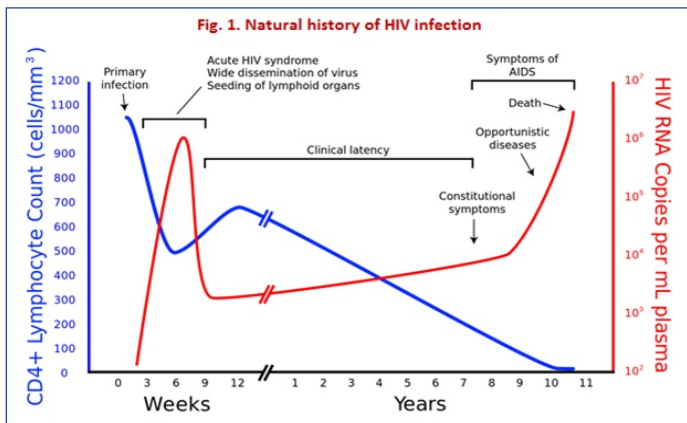
Current status of the HIV pandemic

Global

Data from HIV sero-surveillance and follow-up of PLHA showed that HIV infection was mainly a sexually transmitted disease with a long asymptomatic period followed by relatively rapid deterioration of immune status and increased risk of infection (Fig.1); AIDS represented the terminal stage of HIV infection. UNAIDS estimated that in 2016 there are about 36.7 million PLHA of whom 2.1 million are children below 15 years of age. The prevalence of HIV infection in adults in different regions is given in Fig.2 and the incidence of new infections and changes from 2010 to 2016 are given in Fig.3. There has been a steep reduction in the number of new infections; there were an estimated 1.8 million new infections in 2016, of which about 160,000 were in children. The overall incidence rate for adults 15 to 49 years of age reached a peak of 0.11% in 1997 and decreased to 0.05% in 2012. The greatest decrease in HIV incidence is among

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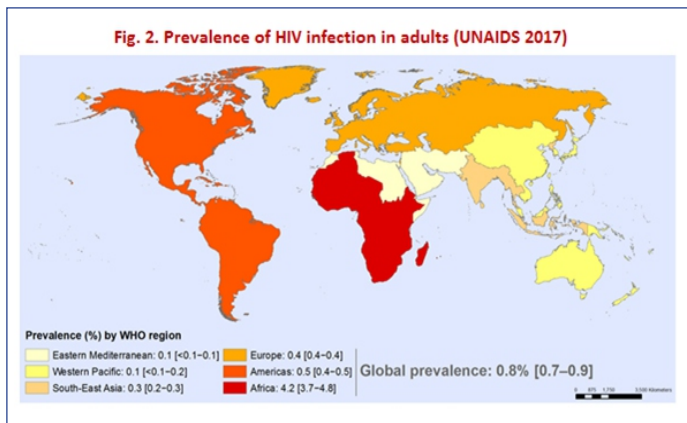
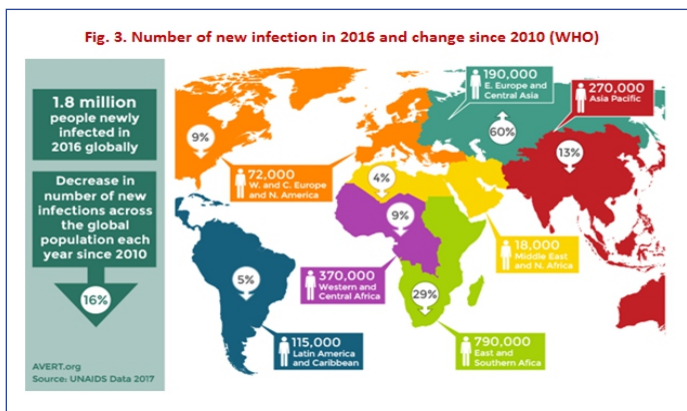


children, a reduction of 52% in 10 years. The reasons for the decrease in incidence rates include reduced infectiousness of PLHA because most of them are on anti-retroviral therapy (ART), the expansion of prevention of parent-to-child transmission (PPTCT) programme, and the introduction of harm-reduction programmes focusing on safer sex, and outreach to high-risk populations¹.

In the past 15 years, there has been a steep increase in number of persons getting ART coverage (Fig.4). India has played an important role in scaling up of ART in India as well as globally by making generic ART drugs available at an affordable cost, thereby contributing to the achievement of Target 7 of goal 6 of MDG across the world. An estimated 17 million people accessed life-saving anti-retroviral medicines at the end of 2015, with an additional 2 million people gaining access over the next 12-month period. Increased access to ART has averted an estimated 5.2 million AIDS-related deaths in low and middle-income countries from 1995 to 2010, with a 28% reduction in deaths from 2006 to 2012. Scale-up of ART since 2010 by many of the world's most affected countries has reduced AIDS-related deaths from 1.5 million in 2010 (CI 1.3 million-1.7 million) to 1.1 million (CI 940,000-1.3 million) in 2015. The gains were greatest in the world's most affected region, eastern and southern Africa, where coverage of ART increased from 24% (CI 22%-25%) in 2010 to 54% (CI 50%-58%) in 2015, reaching a total of 10.3 million people (Fig.5)¹. There has been substantial increase in longevity and improvement in quality of life with increase in access to ART. However, it is a matter of concern that even in U.S, with the oldest and the most comprehensive AIDS control programme in the world, there have been substantial gaps in accessing ART and the goal of viral load suppression has been achieved in less than a third of PLHA (Fig.6)².

India

Data from ICMR's sero-surveillance for HIV infection between 1986

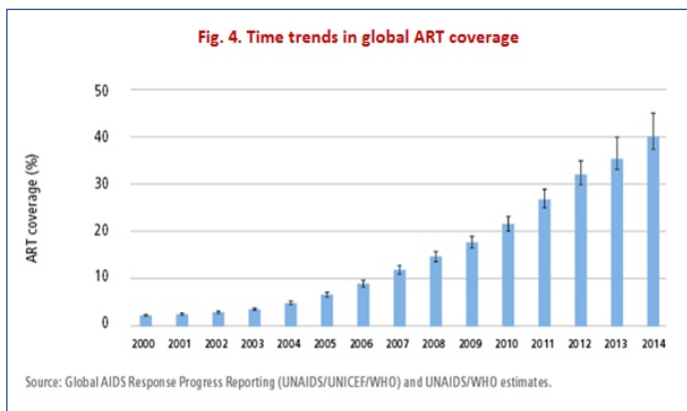


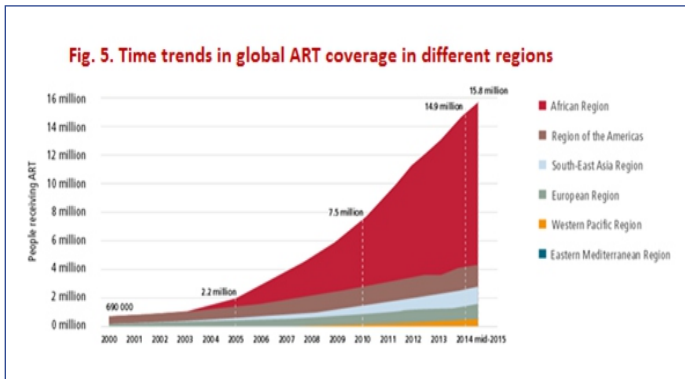
and 1991 showed that:

- HIV infection was present in all the recognised high-risk groups (HRGs) and the general population in all states, both in urban and rural areas
- the prevalence of HIV infection was not high even in the HRGs; the highest prevalence was reported in IV drug users; the second highest prevalence was reported in female sex workers;
- the prevalence of HIV infection in the general population was very low, and,
- the transmission of HIV infection in India was occurring through all known modes of transmission(Fig. 7)³.

Two major determinants of magnitude of HIV infection are size and overlap of HRG, bridge group and general population. In India the relatively small size of high-risk and bridge group (men and women who have sex with commercial sex workers and also with their spouses) have ensured that the infection rates in the general population remained low (Fig. 8)³.

India had the advantage of initiating the NACP very early in the course of the HIV epidemic, when the prevalence of HIV infection was low. Prevalence of HIV infection (Fig.9) was low right from the early 1990s and there has been a progressive reduction in the prevalence of HIV infection. Sentinel surveillance has shown that there was a fall in sero-prevalence of HIV infection in HRG [injecting drug users (IDU), female sex workers (FSW), men who had sex with men (MSM)] and pregnant women (ANC) representing the general population (Fig.10). There has been a near-elimination of blood-borne and mother-to-child HIV infection. The estimated prevalence of HIV infection in adults over 15 years is shown in Fig. 11. The peak was seen in 2000-01 and since then there has been a steady decline in the prevalence of HIV infection in adults. Ranking of states according to the prevalence of HIV infection is shown in Fig. 12. All states, including the high-prevalence states, have reported a fall in



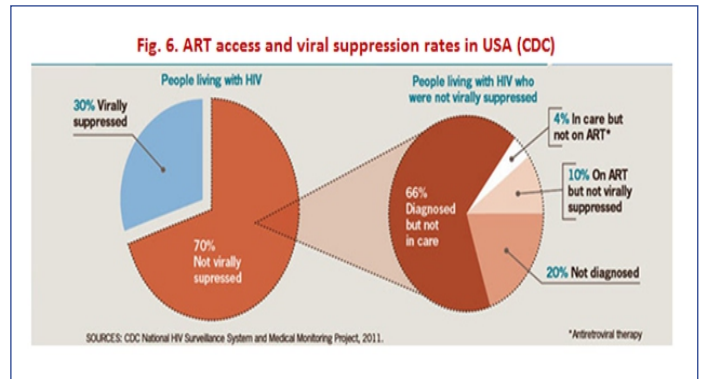
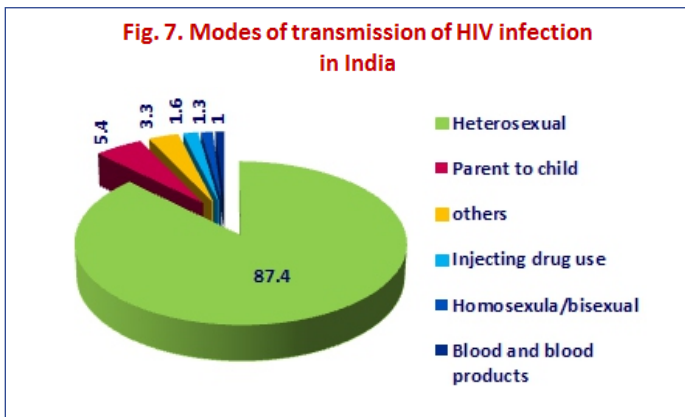


adult HIV prevalence. The number of PLHA has declined from 24 lakhs in 2009 to 20.9 lakh in 2011. Time trends in the incidence of HIV infection in adults and children in India are shown in Fig. 13. India has achieved the MDG targets for reduction in HIV infection rates⁴.

In India, ART is provided totally free of cost; there has been a huge increase in PLHA who are receiving ART; in 2014, over 8 lakh PLHA had accessed ART (Fig. 14). It is estimated that about 1.48 lakh people died of AIDS related causes in 2011 in India. Deaths among HIV-infected children account for 7% of all AIDS-related deaths. ART has led to a 29% reduction in the estimated annual AIDS-related deaths in the country between 2007-2011 (Fig.16). It is estimated that the scale-up of free ART since 2004, has saved cumulatively over 1.5 lakh lives in the country till 2011. The current scale-up of ART services is estimated to avert around 50,000-60,000 deaths annually in the next five years⁴. It is noteworthy that India has successfully provided treatment for HIV infected persons without any adverse impact on treatment of other ailments in the country, and that the AIDS epidemic had no impact on the rate of reduction in under-nutrition and mortality rates in India.

Nutrition and HIV infection

By 1990 on-going global epidemiological studies had documented the natural history of HIV infection. Long-term follow-up of HIV-infected persons detected in the asymptomatic period showed that, contrary to the initial belief, HIV infection is a chronic disease with a long, asymptomatic period, and that immune deficiency, infections, and wasting occurred only in the terminal phases (Fig 1). Studies in different phases of HIV infection were undertaken to document the effect of HIV infection on nutritional status and the effect of nutritional status on the course and outcome of the infection. These studies showed that there are major differences in the nutritional status of HIV-infected persons depending upon whether they are citizens of developed or developing countries, their economic status, route of infection, response to the virus, stage of the disease at the time of detection, type of opportunistic infections and access



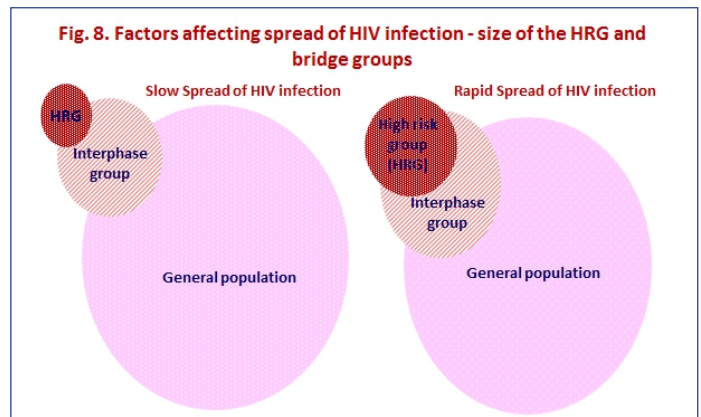
to ART, essential healthcare and nutrition services. All these factors and their complex interactions have to be taken into account in assessing HIV infection-nutrition interactions and planning appropriate interventions to sustain/improve the nutritional status of HIV-infected persons⁵.

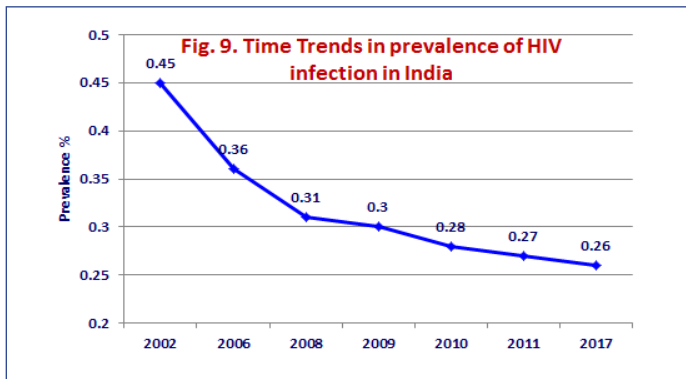
Nutritional requirements of HIV-infected persons

Numerous studies both in developed and developing countries have investigated energy requirements, nutritional status and body composition of HIV-infected persons, from the asymptomatic phase through symptomatic phases. Resting energy expenditure (REE) has been shown to be higher by 10% even in the asymptomatic phase, both in adults and children. REE levels are higher in persons with secondary opportunistic infections. Energy needs increase by an additional 20-50% during convalescence after a severe infection. Whole-body protein turnover has been reported to be ~25% higher in untreated HIV-infected individuals as compared to HIV-negative controls. The increase in protein turnover is positively correlated with increase in REE. Increased protein requirements in HIV infection can be met by a balanced diet designed to meet the total energy requirements (increase of 12 to 15% of the total energy intake)⁵.

Weight loss in HIV infection

Persons, who had been optimally nourished prior to being infected with HIV, may continue to be well-nourished and remain asymptomatic for longer periods. Weight loss in HIV infection could be because the increased energy needs are not being met, due to a variety of reasons including poverty and food insecurity (reported to be a major problem in some Sub-Saharan countries), loss of appetite and decreased absorption of nutrients. Malabsorption of fat caused by gastrointestinal infections is another important factor. The magnitude of weight loss varies among individuals, with a ≥10% loss over the period of a year being common in the era when ART was not





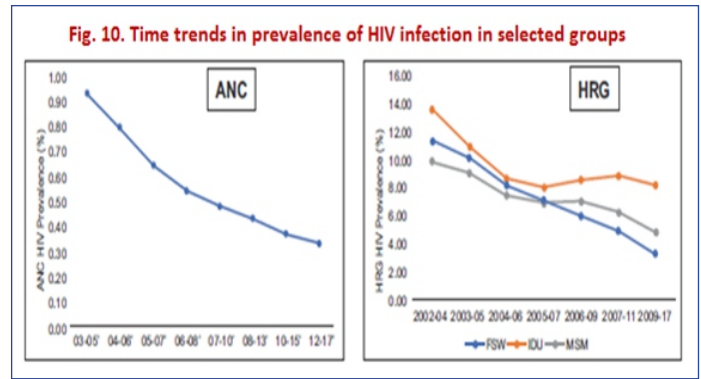
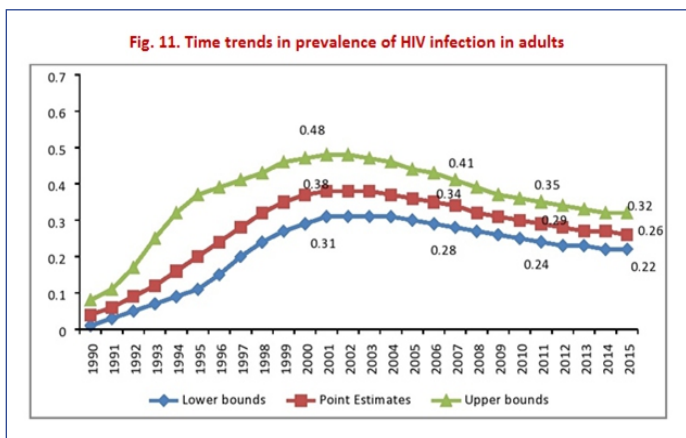
widely used. Acute weight loss is often seen in persons with opportunistic infections. In India, HIV-TB co-infection is a major cause of weight loss in PLHA; effective treatment of TB has been shown to reverse the weight loss. Successful treatment of opportunistic infections and adequate food intake does reduce wasting but in persons with low CD count, wasting can recur with the next episode of opportunistic infection⁵.

Effect of nutritional status on course and outcome of HIV infection

Research studies both in developed and developing countries have shown that under-nutrition, whether due to food insecurity or infections, hastened the fall in CD4 counts and progression of the disease. If the increased energy and protein needs are not met, fat and protein stores are used to meet the body's energy requirements, resulting in weight loss in adults and growth failure in children. The loss of body protein could further compromise the immune system of the HIV-infected individual. Low BMI at the start of ART is an independent important predictor of early mortality. Available meagre data indicate that anaemia and other micro-nutrient deficiencies are associated with fall in CD 4 counts and increased risk of infections⁵.

HIV infection in pregnancy

Initial reports, mainly from Sub-Saharan countries, suggested that HIV-infected pregnant women gain less weight and experience micro-nutrient deficiencies more frequently than uninfected pregnant women. However when comparisons were made between pregnant women of similar socio-economic status, there were no significant differences in weight gain, mid-upper arm circumference, and triceps fat-fold thickness between asymptomatic pregnant women at early stages of HIV infection and HIV-negative women. A high proportion of HIV-positive women had anaemia along with low or deficient folate or vitamin A levels. This could be because HIV-



positive women in developing countries may not be consuming a balanced diet rich in micro-nutrients, and may not be receiving pre-natal vitamin and mineral supplements. Most studies have reported that under-nourished HIV-positive pregnant women had higher viral loads and lower CD4 counts. Some studies have documented that a higher proportion of HIV-positive pregnant women who had low or deficient levels of folate, albumin, and vitamin A, had increased viral loads and decreased CD4 counts. Optimal nutrition for HIV-infected women during pregnancy and lactation improves weight gain and birth outcomes. Pregnancy does not hasten the progression of HIV infection⁵.

HIV infection and lactation

There were no differences in the extent of weight loss between HIV-positive lactating women and HIV-negative lactating women. The transmission of HIV from a HIV-positive mother to her child can occur during pregnancy, labour, delivery or breast-feeding. In the absence of any intervention, transmission rates range from 10 to 30%. In the mid-1980s the guidelines from the WHO and the Centre for Disease Control (CDC), U.S., suggested that, in order to prevent HIV infection transmission through breast milk, sero-positive women should not breast-feed their offspring. This was an appropriate recommendation for developed countries where the majority of babies were receiving formula feeds and formula feeds are generally affordable, accessible and safe. However, these guidelines were not appropriate for developing countries.

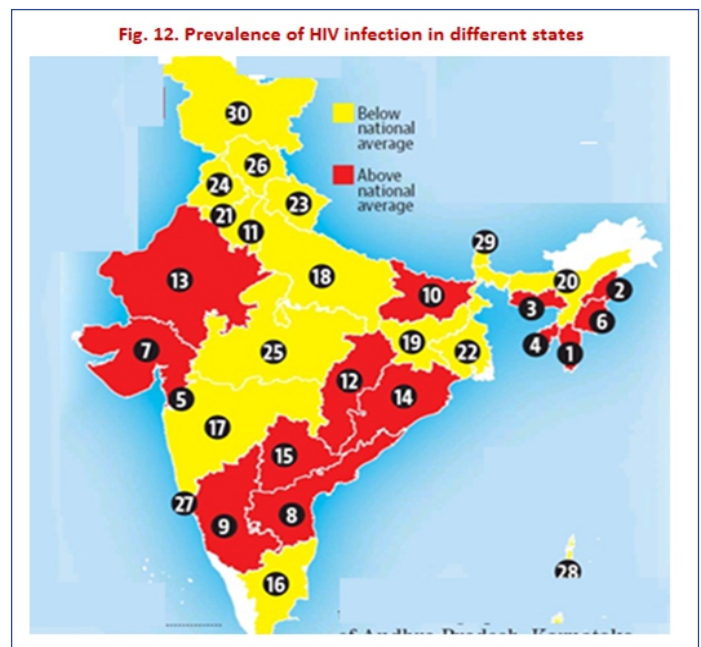
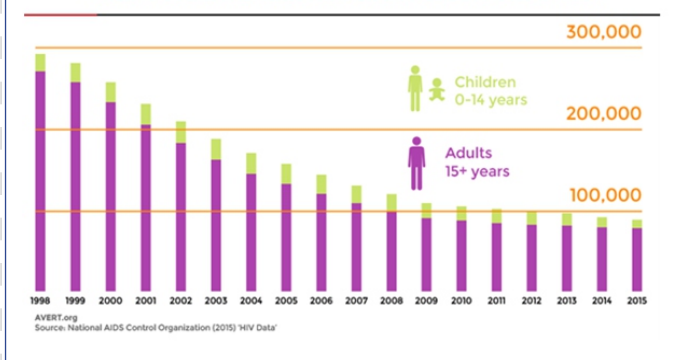


Fig. 13. Time trends in estimated new infections in children and adults (India)



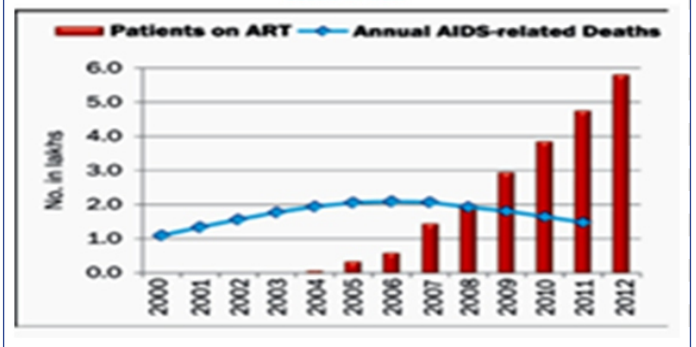
Following the birth of an infant to a sero-positive mother in 1987, India followed the WHO guidelines, and provided the family infant milk formulae totally free of cost. The mother was counselled on how to prepare the formula and feed the infant. Subsequently this procedure was followed in other cases and the mother-child dyads were followed-up closely. Within a year it became obvious that these infants were experiencing repeated infections and showed severe growth faltering by the age of 6 months. Similar findings were reported from other mother-child dyads in other developing countries. The ICMR expert group weighed the risk of improper formula feeding against that of transmission of the virus through breast milk, and recommended that breast-feeding, which is known to protect against morbidity and under-nutrition, should be promoted in sero-positive women and also all women whose HIV infection status was not known because they had not been screened for HIV³. India successfully spearheaded efforts for modification of the WHO guidelines to include the perspective of developing countries. The WHO revised the guidelines for infant feeding stating that infant feeding practices recommended to mothers known to be HIV-infected should support the greatest likelihood of HIV-free survival of their children and not harm the health of the mothers. To achieve this, prioritization of prevention of HIV transmission needs to be balanced with meeting the nutritional requirements and protection of infants against non-HIV morbidity and mortality. The guidelines recommended that:

- for women who are known not to be infected with HIV, and for women whose infection status is unknown: protect, promote and support exclusive breast-feeding for 6 months;
- when replacement feeding is acceptable, feasible, affordable, sustainable and safe, HIV-positive mothers may avoid breast-feeding;
- to minimise HIV transmission risk, breast-feeding should be discontinued as soon as feasible; and,
- when HIV-infected mothers choose not to breast-feed from birth or stop breast-feeding later, they should be provided with specific guidance and support for at least the first 2 years of the child's life to ensure adequate replacement feeding.

India's efforts to ensure that breast-feeding is the norm for all mothers irrespective of their HIV status (known or unknown) has saved the lives of thousands of infants and prevented deterioration in their nutritional status.

In the last decade screening of pregnant women for HIV infection and providing them with ART has become the standard practice both in developed and developing countries. Currently the guidelines envisage that all pregnant women should be screened for HIV infection and all those found to be sero-positive have to be put on continuous ART. This has a major impact in terms of minimizing the mother-to-child transmission during pregnancy, labour and lactation. Earlier international guidelines emphasized on exclusive

Fig. 14. Time trends in number of persons on ART and AIDS related deaths in India



breast-feeding and counselled against mixed feeding in the first six months and recommended the stopping of breast-feeding at 12 months. Under the current guidelines both the mother and the infant receive ART irrespective of the HIV status of the child; therefore the risk of HIV infection during lactation has been minimized if not eliminated. Currently all women irrespective of HIV status are advised to follow the national guidelines on breast-feeding practices: exclusive breast-feeding for the first six months, introduction of appropriate complementary feeding from six months and continued breast-feeding as long as they can - up to two years⁵.

HIV infection and under-nutrition in children

Under-nutrition and growth faltering are common in HIV-infected children⁷; under-nutrition adversely affects immune status and survival. In India, even among the "normal population", intrauterine growth retardation is common and one-third of infants are born with low birth weight; intrauterine growth may be compromised to a greater extent in children born to HIV-infected women. However so far there have not been any studies to document the effect (if any) of HIV infection on birth weight. In developing countries, poor infant and young child feeding practices and diarrhoea are two major factors contributing to poor growth and under-nutrition in infancy (both in HIV-infected and HIV-negative children). Prevention, early detection and treatment of diarrhoea may enhance childhood growth and survival in children with HIV. Under-nutrition in HIV-infected children is associated with rapid progression of the disease and poor outcomes. The available data indicate that energy supplementation to HIV-infected children improves weight gain but does not reverse deficits in height.

Increased access to ART has made an enormous contribution towards improving the health status and survival of HIV-infected children. ART postpones progression of the disease and fall in CD4 counts, prevents deterioration in health and nutritional status, and prolongs life⁸. However, the use of ART is not without side-effects. ART can adversely affect body weight and linear growth in children. Abnormalities in body fat, lipids, insulin and bone metabolism have been reported in children receiving ART⁸.

Priority areas requiring strengthening under HIV/AIDS control programmes for improving the nutritional status of children born to sero-positive mothers include:

- regular growth monitoring using the Mother Child Protection Card for early detection and effective management of growth faltering;
- nutrition training for health service personnel so that they can provide nutrition and health education; and,
- early detection and management of illnesses, especially diarrhoea.

HIV infection and household food security

In Africa in the twentieth century, HIV/AIDS had a devastating impact on agriculture and food production at the national level, and livelihoods and food security at the household level. In India, at the state and national levels, agricultural and industrial production continued to grow and the country remained self-sufficient in food production. In fact, in the past decade agricultural production has continued to increase and India has become a food exporting country. However HIV infection, especially in the bread-winner of the family, had an adverse effect on employment, earning and household food security. Poverty rates were reported to be higher among household affected by HIV/AIDS as compared to unaffected families. Income loss is substantially higher among the poorest households which depend upon daily wages for manual labour. HIV infection and death of the earning member of the family can perpetuate household poverty and result in under-nutrition of the survivors⁵.

Nutrition and AIDS

In the early 1980s AIDS epidemic was characterized by wasting and opportunistic infections of the affected persons. In mid-eighties, WHO drew up the case definition of AIDS for use in situations where HIV testing facilities were not widely available, (such as in Sub-Saharan Africa); wasting was the major essential sign for diagnosis of AIDS both in adults and in children. In persons with clinical signs of wasting and opportunistic infections, HIV antibody testing was to be done for confirmation of the diagnosis. Where tests were not readily available the clinical criteria for case definition were to be followed for diagnosis and management. In the 1990s most of the data on the effect of nutritional status and nutrition interventions on the course and outcome of AIDS were based on studies carried out on the treatment of AIDS patients in developed countries. AIDS-associated weight loss and wasting were shown to be independent contributing factors to poor clinical outcomes in AIDS. Since then these findings have been confirmed in developing countries also. The focus of interventions for management of AIDS was on combating infections and improving nutritional status⁵. However, it is now realised that AIDS is the terminal phase of HIV infection and the asymptomatic phase of HIV infection may not be associated with either infection or under-nutrition. It is also realised that ART can bring about major changes in nutritional status of individuals.

Nutrition and ART

ART is associated with metabolic alterations both in adults and children^{5,8,9}. These include increased energy requirements, increased insulin resistance, abnormally high levels of blood cholesterol and triglycerides, and osteoporosis and osteopenia. Both wasting and lipodystrophy have been reported in long-term ART users. BMI at the time of entry for treatment is an independent and significant predictor of mortality in HIV-infected persons receiving ART. Under-nutrition and micro-nutrient deficiencies have an adverse effect on response to ART. Loss of body fat, called lipodystrophy has been reported both from developed and developing countries in ART users. Fat loss generally occurs in the cheeks, buttocks, arms and legs. Lipodystrophy with overall increase in body fat has been widely reported in long term ART users; lipodystrophy can occur along with loss of muscle mass. In addition to ART, factors such as age, gender & weight before HIV infection, genetic predisposition, length of time the person has been HIV-positive, and severity of the disease influence the development of lipodystrophy^{5,10,11}. Lipodystrophy and abdominal adiposity are associated with biochemical changes such as increase in triglycerides and cholesterol, and increased insulin resistance; all these have been shown to be associated with increased risk of cardiovascular diseases (CVD)^{10,11}.

In India currently there is no consolidated data on the prevalence of

lipodystrophy or lipotrophy in long-term ART users or factors associated with their development. The fact that Indians are prone to the “metabolic syndrome” (combination of obesity, hypertension, dyslipidaemias, insulin insensitivity) has been well documented. The presence of the metabolic syndrome in ART users can increase the risk of morbidity and mortality due to CVD. With wider and longer duration of the use of ART, larger numbers of persons living with HIV may develop metabolic syndrome and face adverse health consequences associated with it. Early identification of changes in BMI and adiposity and interventions to combat them through modification of dietary intake and ensuring adequate exercise may be required.

Effect of food supplementation on course and outcome of HIV infection

Achieving and maintaining optimal nutrition is an important adjunct in the clinical care of patients infected with HIV. Good nutrition improves immune function, limits disease-specific complications and improves quality of life and survival. Approaches towards improving the nutritional status of HIV-infected persons have varied widely from food-based interventions (diets high in energy, protein, or fats), oral supplements with specific nutrients, enteral and total parenteral therapy, and the use of appetite stimulants and anabolic hormones. Large-scale humanitarian food assistance has done much to improve the nutritional status of HIV-infected persons, both in developed and developing countries⁵.

The Tuberculosis Research Centre, Chennai, conducted a prospective interventional study between June 2005 and December 2007 to evaluate the effect of macro-nutrient supplementation in HIV-infected adults. Patients at one unit of TRC received nutritional counselling and standard care; patients at the second unit received in addition a macro-nutrient supplement providing 400 Kcal and 15gm of protein daily. There was some increase in body weight, BMI, mid-arm circumference, fat-free mass, and body cell mass in the group that had received supplements. There was no change in CD4 count in the group receiving supplements, whereas CD4 count decreased in the control group. After adjusting for baseline differences, none of these changes was statistically significant, suggesting that macro-nutrient supplementation did not result in significant improvement either in nutritional status or in the course of the HIV infection¹². A similar study on nutrition supplements from Vellore also failed to show any significant improvement following food supplementation¹³.

A Cochrane review found only eight small, randomised controlled trials (RCTs) (combined sample sizes for the various outcomes range from 128 to 178 participants) in which the effect of macro-nutrient supplementation was compared with that of placebo or of no nutritional supplementation. This review found that balanced nutritional supplements aimed at improving energy intake by 600-960 kcal/day did result in improvement in energy and protein intake; specific nutritional supplements increased body weight and decreased HIV viral load, but the clinical outcome of HIV infection remained unchanged. Variations in the nutritional composition of the supplements, differences in the disease stage of the participants (which can significantly affect intake and absorption of food), exclusion of patients with acute opportunistic infections (who are most prone for weight loss and most likely to experience improvements in nutritional status), are some of the major limitations of these RCTs¹⁴. All these trials were conducted in either North America or Europe and evaluated well-nourished males and females between the ages of 30 and 50 years who were receiving ART. More studies are needed in low-income countries, and particularly in children, to explore the effect of macro-nutrient supplementation in conjunction with ART.

Cochrane systematic review have been done for studies carried out to determine the effect of macro-nutrient interventions to provide

protein and/or energy, or test the effect of specific macro-nutrients (i.e. as amino acids, whey protein concentrate or Spirulina), given orally, on morbidity and mortality in adults and children living with HIV infection. The review, based on fourteen small trials, found limited evidence that balanced macro-nutrient formulae increase protein and energy intake. There was no evidence that such supplementation translated into reduction in disease progression or HIV-related complications, such as opportunistic infections or death. All these indicate that the impact of food supplementation on nutritional status and course and outcome of HIV in PLHA is very limited.

Effect of micro-nutrient supplementation on course and outcome of HIV infection

HIV infection may impair micro-nutrient intake and alter micro-nutrient requirements. Micro-nutrient deficiency may accelerate the progression of the disease, increase morbidity, and increase the risk of mother-to-child transmission. Both in developed and developing countries micro-nutrient supplements have been widely used in the clinical care of HIV-infected persons in various stages of the infection. However, there is very little evidence to confirm the beneficial effects of micro-nutrient supplementation on the course or outcome of the disease. With increasing use of ART and Highly Active Anti-retroviral Therapy (HAART) now, the impact of these prolonged drug therapies on micro-nutrient status has to be taken into account while assessing the effect of micro-nutrient supplementation⁵.

A recent Cochrane review examined the effect of micro-nutrient supplements on mortality and HIV-related morbidity of HIV-positive adults using data from 33 trials with 10,325 participants. Ten trials compared a daily multiple micro-nutrient supplement to placebo in doses up to 20 times the dietary reference intake, and one trial compared a daily standard dose with a high daily dose of multivitamins. Nineteen trials compared supplementation with single or dual micro-nutrients (such as vitamins A and D, zinc, and selenium) to placebo, and three trials compared different dosages or combinations of micro-nutrients. Routine multiple micro-nutrient supplementation had very little impact on mean CD4 cell count, mean viral load or mortality in PLHA. The analyses of the available trials did not reveal substantial consistent clinically important benefits with routine multiple micro-nutrient supplementations in PLHA¹⁵. However micro-nutrient supplements are indicated to correct existing deficiencies in people living with HIV who have specific deficiencies or where the person's diet is insufficient to meet the recommended daily allowance of vitamins and minerals.

Use of iron supplementation has been reported to have adverse effects (due to oxidative stress?) on the course of HIV infection, in settings where iron deficiency is not a problem. The applicability of the finding to countries with widespread iron deficiency and anaemia is limited. Iron deficiency and anaemia are associated with immune-depression¹³. There have been no reports from India on the effect, if any, of anaemia on progression of HIV infection and whether detection and treatment of anaemia has any positive impact on the course and outcome of HIV disease. This is a priority area for research, especially in India, where prevalence of anaemia in men and women during reproductive age is very high.

Micronutrient supplementation in pregnant women

In Africa, several micro-nutrient supplementation studies have been carried out in HIV-infected pregnant women. Micro-nutrient deficiencies were commonly seen in pregnant women, supplementation through antenatal clinics was relatively easy, and the outcome of pregnancy as well as mother-to-child transmission rates could be readily measured and documented. There are unconfirmed reports that high doses of vitamins B, C and E

supplements may reduce mother-to-child HIV transmission. One trial showed that a daily high-dose multi-vitamin supplement may reduce adverse pregnancy outcomes and mother-to-child transmission, and considerably reduce progression of HIV infection in pregnant women. One unconfirmed study showed that high dose supplementation with vitamin A and β -carotene actually increased mother-to-child HIV transmission.

A Cochrane review of randomized trials¹⁶ of micro-nutrient supplementation in pregnant women reported that the available data on the effects of micro-nutrient supplementation on the course and outcome in HIV infection in pregnancy are inconclusive both as regards supporting the claims of beneficial effects and allaying the concern that supplementation may have adverse consequences. Part of the observed variation in outcomes might be attributable to the pre-existing micro-nutrient intake and status of the patient, whether or not the woman was also receiving ART, and the stage of HIV infection. In addition, the levels of other micro-nutrients may modify the effects of specific micro-nutrient supplementation. The sheet-anchor of the strategy for prevention of mother-to-child transmission and for treatment of maternal HIV infection during pregnancy is ART. In developing countries where micro-nutrient deficiencies are common, supplementation can be used to correct existing deficiencies.

Micro-nutrient supplementation in children

A Cochrane review¹⁷ based on evidence from randomized clinical trials in HIV-infected children and non-HIV-infected subjects shows that the administration of large doses of vitamin A (a single large dose of 50 000 IU before 6 months; a single dose of 100,000 IU between 6 and 11 months; a single dose of 200 000 IU every 6 months from the age of 12 months onwards) reduces diarrhoea-related morbidity and mortality and all-cause mortality in severely vitamin A-deficient under-five children. In many developing countries sub-clinical vitamin A deficiency is common, and vitamin A supplementation may be effective as an adjuvant treatment in such persons; however, its impact in those who do not have vitamin A deficiency has to be assessed. Appropriate treatment of diarrhoea is essential in all children irrespective of their HIV status.

The way forward

In the eighties, AIDS appeared to be an acute disease with severe wasting, high morbidity and high case fatality. The health sector and scientific community responded vigorously to the emergence of this epidemic; within the next five years treatment protocols for AIDS were drawn up, the organism responsible was identified and tests for detection of infection were developed. Over the next five years global sero-surveillance and AIDS reporting networks were developed, natural history of HIV defined and ART for viral load reduction developed, global and national AIDS control programmes were evolved. The global and national AIDS control programmes had two components:

- HIV transmission prevention through behavioural modification, prevention of blood borne transmission, PPTCT and prevention of accidental transmission of HIV infection in health care settings and,
- early detection and effective management of PLHA.

Effective implementation of these resulted in the world achieving the MDG target of halting the HIV epidemic – within three and a half decades after its detection.

India was fortunate because HIV infection reached the country late and sero-surveillance for HIV infection led to the detection of infection even before the first case of AIDS was reported. As the dimensions of the epidemic unfolded, rational, evidence based interventions which could be implemented within the existing

health system, were initiated. The National AIDS Control Programme (NACP) continued and scaled up all these interventions. Effective implementation of a multi-pronged, rational strategy for HIV infection and dedicated work done by committed professionals belonging to government and voluntary sectors resulted in containment and control of infection right from the initial stages. The cultural ethos of the country and responsible behaviour of the population played a major role in ensuring rapid decline in new infection and steep reduction in prevalence of infection within two decades after the initial detection of HIV.

Encouraged by these results the SDG target is to strive and eliminate HIV infection by 2030. We now know that HIV infection is a chronic disease with myriad of health and nutritional manifestations, requiring lifelong treatment and life-style modification. Research studies exploring lifelong ART after detection of HIV infection¹⁸, ART for prevention of infection in sero-discordant couples, in the post-exposure period and in high risk groups unable to modify their life styles have shown encouraging results¹⁹. There is advocacy for scaling up these interventions. But these interventions may bring in their own sets of problems in terms of side effects of drugs, increasing drug resistance, compliance problems with therapy for decades and cost of care. The progress towards SDG targets will be determined by the commitment and coordination between research workers, health planners, policy makers and health care providers, and last but not perhaps the most important the people themselves.

The author is Director, Nutrition Foundation of India. The article is based on the C Ramachandran Memorial lecture she delivered at NFI on 28.11.2017.

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FOUNDATION NEWS

- The Annual Foundation Day of NFI was celebrated on 28th November, 2017. On this occasion Dr. Prema Ramachandran delivered the C. Ramachandran Memorial Lecture on “HIV infection and nutrition” at Nutrition Foundation of India New Delhi.
- The NAMS-NFI symposium on “Food fortification for improving micronutrient intakes” was held on 29.11.2017 at Kamla Raheja Auditorium, JS Bajaj Centre for Multi-professional Education, NAMS House, New Delhi

NUTRITION NEWS

- The 49th Annual National Conference of the Nutrition Society of India was held from 2-4 November, 2017 at Assam Agricultural University, Jorhat Assam.
- The 50th Annual National Conference of Indian Dietetic Association was held from 18-20 December, 2017 at Science City, Kolkata.