

I N T R O D U C T I O N

INTRODUCTION

The major nutritional problems facing the world's population today are the appreciable prevalence of under-nutrition in the developing countries and over nutrition in the developed countries, not to mention the effects of deficiencies of specific nutrients such as protein, calorie, vitamin A, thiamine, niacin, iron and excesses of certain others like fluoride and sugar (Moore, 1957; 1968; Patwardhan, 1961; Liang Chi-Chin, 1962; Champakam et al, 1968; Jolly et al, 1968; Gopalan, 1969; Gopalan and Srikantia, 1973; McLaren et al, 1973; Reiser et al 1981, Bagchi, 1983).

Although undernutrition and malnutrition are prevalent at all ages, the consequences of undernutrition are particularly serious during the growth period especially the fetal growth and those of overnutrition during adult life. The former is well documented in terms of growth retardation, increased morbidity and mortality, impairment of different facets of development (Dreizen et al, 1961; Garn et al, 1969; Craviotto et al, 1971; Monckeberg et al, 1972; McLaren et al, 1973; Gopalan and Srikantia, 1973; Dobbing, 1974; Bengoa, 1975; Bagchi, 1983; Pratapkumar, 1983;) and the later with the prevalence of obesity and degenerative diseases such as atherosclerosis, diabetes, hypertension and so on in adults (Bierman et al, 1968; Keys et al, 1972; Nolen, 1972; Bauchex, 1976; Abraham et al, 1976; Gupta et al 1978; Verma et al 1986. Thus these two factors (undernutrition and overnutrition) can affect

the two facets (fetal period and adulthood) of life and reduce the life span of an individual. The present investigation is thus chosen with interest on these two divergent groups at Trivandrum (Kerala) to study the nutritional status ~~with a~~ few selected biochemical parameters that might be altered because of the unique pattern of the diet consumed in this region.

Southern states in India and Kerala in particular, has a unique dietary pattern. The population's staple food here is parboiled rice of the red variety and tapioca (also known as Cassava, Yuca and Mamioca) the proportion of which vary in the low (LIG) and high (HIG) income groups. Among the non-vegetarians again the consumption of fish and pork makes a difference between the HIG and LIG. The cooking fat is also different in that it is coconut oil and coconut which contain high saturated fats and Low tocoferol content (Gopalan et al, 1978).

Apart from the major differences in the proximate principles, the diet is also poor in magnesium mainly due to the soft water in Kerala. Tapioca and rice also being poor sources of magnesium (Gopalan et al 1978, Rajalakshmi and Rama Krishnan 1980) may contribute to a lowered magnesium status in these populations.

Thus the objectives of this investigation was to see the effects of this diet on fetal growth and outcome in

relations to maternal nutritional status and 2) aging changes in relation to diet that may alter serum components and somatic parameters. The following review is hence discussed in two sections -

Section I - Fetal growth in relation to maternal nutrition.

Section II - Aging changes in relation to diet.

SECTION I: Fetal Growth in relation to Maternal Nutrition

Fetal growth largely depends on an adequate supply of nutrition and the ability of the fetus to utilise this supply. Under normal physiological conditions anabolic processes are dominant during pregnancy (Hyttén and Leitch, 1971; Calloway, 1974; Cf. Naismith, 1980). However maternal body weights may decrease during the first few weeks of pregnancy because of nausea and vomiting resulting from the anatomic, physiological and metabolic adjustments that take place at that time. The appetite subsequently increases to a peak during mid-pregnancy and then declines again towards term. It is reported that the American and Western European middle-class women increase their energy intake by about 200 calories over the pre-pregnancy level (Lunell et al, 1969)

Poor women in this country and elsewhere, whose diet is already inadequate in many respects, particularly with regard to

food energy, protein, calcium, vitamin A, riboflavin and ascorbic acid, also do not show perceptably increased food intakes during either pregnancy or lactation (Pasricha, 1958; Bagchi and Bose, 1962; Rajalakshmi and Ramakrishnan, 1969; Rajalakshmi, 1971; Srikantia and Iyengar, 1972) although some studies suggest an increase of about 300 calories on the basis of cross-sectional studies (Sengupta and Bagchi, 1961; Shanker, 1962; Devadas et al, 1964).

In addition to these pregnancy is associated with a decrease in gastric secretions of acid (Murray et al, 1957; Hunt and Murray, 1958) and pepsin (Gryboski and Spiro, 1956) and increased gastric motility and tone with a consequent delay in gastric emptying time (Parry et al, 1970). Despite these changes, pregnant women are found to show more efficient absorption of several nutrients including protein, iron & calcium, which will be discussed later.

In order to meet the demands of the growing fetus several physiological adjustments take place in the maternal system. One of such is the expansion of blood volume resulting in hemodilution because of the relatively greater expansion of plasma volume which begins around conception to reach a peak at 28-32 weeks of gestation (Hyttén and Leitch, 1971; Peck and Arias, 1979). The extent of expansion may vary from about 15 to 20% according to Lund (1951). Plasma volume shows a progressive step-wise increase over the non-pregnant state by about 2.3 per cent

in the first trimester reaching to a maximum of 63 per cent at term with a small plateau between 32 to 36 weeks of pregnancy (Rajalakshmi and Raman, 1985). Plasma dilution occurs with regard to some constituents such as plasma proteins and most serum electrolytes (Hyttén and Lund, 1973). Unlike plasma volume, red cell volume does not change till the 20th week of gestation after which a progressive increase is observed (6 per cent at 20 - 28 weeks rising to 50 per cent at 37 - 40 weeks) (Rajalakshmi and Raman, 1985).

Hyttén and Paintin (1963) showed a close relationship between increase in plasma volume and the birth weights of the infant. Women with a history of still births or abortions low birth weight infants show in general a much smaller increase in plasma volume than normal pregnant women (Hyttén and Leitch, 1971). In this connection, in Indian women it is shown that the increase in plasma volume occurs much later than in western women in the last trimester. A close correlation ($P < 0.02$) was also shown between plasma volume after 36 weeks of gestation and birth weight of infant (Rajalakshmi and Raman, 1985). These authors hence suggested that measurement of plasma volume in early pregnancy and at the beginning of third trimester of pregnancy can provide an indication of risk needing intervention.

However, the changes in blood composition cannot entirely be attributed to hemodilution or plasma dilution as

their timings do not always correspond to that of peak changes reported for different constituents. Also hemodilution itself varies from individual to individual (Dave, 1980). For instance, the progress of pregnancy is associated with an increase in lipids, serum vitamin E, hormones such as progesterone, estrogen and prolactin, albumin but not globulin and a fall in blood-glucose, hemoglobin, folate, magnesium and iron (Horwitt et al 1975; Dave, 1980; Hytten, 1980; Naismith, 1980; NIN Ann. Report, 1981; Iyengar, 1982). Reports concerning changes with regard to certain other constituents such as vitamin A and C are conflicting and perhaps depend on pre-pregnant nutritional status as well as nutrient supplies during pregnancy (Young et al, 1946; Rajalakshmi, 1980).

The higher concentrations of several nutrients such as calcium, potassium, phosphorus and magnesium in the fetal serum as compared to the maternal serum suggests a placental transport against a concentration gradient. A greater absorption of these minerals during late pregnancy is reported (Coons and Blunt, 1930; Macy et al, 1930; Duckworth and Warnock, 1942; Beaton, 1960; Iyengar and Apte, 1970; Schinolicar, 1970).

In terms of nutritional stress pregnancy involves the daily transfer to the fetus of approximately 160-170 kilocalories, 1.4 g of protein, 100 mg of calcium, 0.75mg of iron, 10-15 mg of vitamin A, 3-5 mg of Vitamin C, etc., not to mention the metabolic cost of placental transfer and fetal tissue

synthesis as well as metabolism of the fetus (Rajalakshmi, 1980). The daily accretion to the fetus is much greater in the later trimester than in the earlier stages of pregnancy in the case of food energy, nitrogen, calcium, iron, vitamin A, etc., as judged by the rate of fetal growth and balance studies (Mitchell, 1964; Widdowson, 1980).

The values shown in Table-1 are average figures for the entire gestation period. However, the rate of deposition varies at different stages. For instance, the total amount of calcium deposited in the fetus increases progressively with gestation being about 6 g at 6 months and 28.6 g towards term. A similar increase is seen with phosphorus and other constituents. Many constituents such as potassium, calcium, phosphorus and magnesium are found in higher concentrations in the fetal than in the maternal blood (Table 2). The placenta seems to have the capacity to transfer nutrients from the maternal to fetal tissues against a concentration gradient.

During the early stages, the developing organism stores no fat as energy reserve apart from the essential lipids such as phospholipids in the cell membranes. The human fetus contains only about 0.5% of fat until mid-gestation after which triglycerides are stored in the form of adipose tissues. The fat content of the body rises to 3.5% at 28 weeks, 7.5% at 34 weeks, and 16% at term. The amount of fat deposited per day over the last three months of gestation is of the order of 14g (Widdowson, 1969).

TABLE - 1: Changes in body composition during the last trimester of fetal growth*.

	Amount (g) in		Mean daily
	6 months fetus	Full term baby	increment (g)
Weight	1000	3500	27.5
Water	880	2440	17.1
Nitrogen	14	64	0.6
Fat	20	525	5.5
Sodium	2.0	5.7	0.041
Potassium	1.5	6.3	0.053
Chloride	2.2	6.0	0.042
Calcium	5.9	28.6	0.240
Magnesium	0.2	0.8	0.006
Phosphorus	3.6	1.7	0.144
	(mg)	(mg)	(mg)
Iron	64	280	2.4
Copper	3.8	14	0.12
Zinc	17.6	53	0.9

* Taken from:

WIDDOWSON E.M. (1980).

TABLE - 2: Comparison of composition of fetal serum
with maternal serum

	Fetus		Mother at term
	Immature	Full term	
Sodium (meg/l)	140	140	140
Chloride "	105	105	105
Potassium "	10.0	6.8	5.0
Calcium (mg/dl)	9.0	11.0	10.0
Phosphorus "	14.9	5.8	4.0
Magnesium "	2.8	2.5	2.0

Taken from:

WIDDOWSON E.M. (1969).

Serum lipid levels are found to show an initial decline before 12 weeks of gestation and rise thereafter (Peters et al, 1951; Smith et al, 1959; Darmandy and Postle, 1982) with the levels at term being markedly higher than those either at three months or in the non-pregnant state. Maximum lipemia is found to occur between 31 to 33 weeks of gestation according to Kaunitz and McKay (1964) and Katiyar et al (1978) and between 35 and 38 weeks according to Morse et al (1975) and at term according to Darmandy and Postle (1982). It returns to normal after partus according to Morse et al (1975). A similar rise has been found in studies on experimental animals (SVanberg and Vikrot, 1965).

The decrease in serum concentrations of lipids during early pregnancy (Peters et al, 1951; Darmandy and Postel, 1982) was attributed to nausea of pregnancy (Peters et al, 1951) but could well have been due to other factors. Considerable evidence is now available that in nearly all the tissues triglyceride uptake is regulated by lipoprotein lipase and that the activity of this enzyme is a mark of its capacity to remove the triglyceride from the blood. The rise in blood lipids during pregnancy has been sought to be in terms of changes in lipoprotein lipase activity (LPLA). The enzyme activity is shown to rise in adipose tissue during early pregnancy in experimental animals which subsequently fell as gestation progresses (Otway and Robinson, 1968; Scow et al, 1973).

Possible mechanisms in LPLA regulation in pregnancy have been theorised as that the maternal hyperinsulinism in mid-gestation could account for the increased conversion of glucose into adipose tissue fatty acids (Knopp et al, 1973). Hyperinsulinism on the other hand has also been shown to enhance the LPLA activity in adipose tissue (Borensztajn, Samols and Rubenstein, 1972). Conversely in late gestation contra-insulin factors could diminish LPLA by the activation of cyclic AMP and the free fatty acids (FFA) elevation occurs in adipose tissue in late gestation. Also the diminished removal of FFA from circulation results in increased lipids in blood during late pregnancy. These changes in maternal organism are attributed to hormonal effects exerted by the fetoplacental unit (Knopp et al, 1975).

The studies by Humphrey et al, (1980) and Childs et al, (1981) regarding whether the hypertriglyceridemia in pregnancy is due to intolerance of exogenous fat, accumulation of endogenous triglycerides or accumulation of remnants of d /1.006 lipoprotein metabolism showed, that hypertriglyceridemia in fed state is due to an increase in endogenous triglycerides and that remnant lipid accumulation does not appear to contribute to the endogenous hypertriglyceridemia. No intolerance to exogenous (dietary) fat was shown and an unimpaired delivery of exogenous fat to oxidising tissues indicated a maximum glucose availability to fetal growth.

The rise in serum lipids is found in all the three major lipid components namely triglycerides, cholesterol and phospholipids (Peters et al, 1951; Mendez et al, 1959; Morse et al, 1975; Katiyar et al, 1978; Darmandy and Postle, 1982).

The rise in serum lipids during pregnancy raises the question as to what extent they are transported to the fetus. The placenta is believed to be actively engaged in the production and uptake of cholesterol required for producing steroid hormones (Sulimovici and Boyd, 1969) and in the synthesis of fatty acids and lipid-mobilizing substances (Lopez-Santolino et al, 1965). At least 10 - 15 per cent of the maternal cholesterol crosses the placenta to meet the fetal needs (Chevallier 1964).

The protein nutritional status in pregnancy is associated with a net retention in the conceptus of about 36 g of nitrogen which would be equivalent to about 540 g of protein. Protein accretion is estimated to be 0.64 g/day during the first 10 weeks and increases steadily to a daily average of 6.1 g during the last 10 weeks which is also the period of maximum fetal weight gain (Thomson and Hytten, 1966; Hytten and Leitch, 1971). It was fashionable to recommend high protein requirements during pregnancy but recent years have seen a scaling down of protein allowances. Although pregnancy may impose an additional net burden of about 900 g of protein or more (Thomson and Hytten, 1966), this extra requirements of protein is likely to be

supplied by about 5-10 g protein/day throughout pregnancy. This additional requirement could well be met by diets which are satisfactory with regard to protein for the non-pregnant women as nitrogen retention is more efficient during pregnancy. In studies carried out in this laboratory, on the low income group the urinary excretion of nitrogen is found to decrease from about 4.5 to 4.0 g/day in late pregnancy (Dave, 1980; Rajalakshmi and Ramakrishnan, 1984). In Kerala, where the diets are poorer with regard to protein the fall in urinary nitrogen was found to be greater, corresponding values being 3.7 and 2.3 g/day. A number of studies show that women with a pre-pregnant weight of 45 kg and consuming 39 - 40 g of protein per day are found to retain adequate amounts of nitrogen (Mitchell, 1962; Venkatachalam, 1962; Thomson and Hytten, 1966; Rajalakshmi and Ramakrishnan, 1969).

It is now generally agreed that when a women has been regularly on an adequate diet before pregnancy, she is not likely to require much in the way of mineral supplementation during pregnancy. However, the supply of some minerals such as iron and calcium may become critical for those whose diets are already poor (Woollan, 1981). In recent years it is being realized that deficiency of magnesium during pregnancy might lead to prematurity, teratogenicity and fetal resorption and during lactation to maternal weight loss (Hurley & Gosen, 1971; Hurley 1976, NIN Annual Report, 1980).

Magnesium is the fourth largest mineral constituent of the human body after calcium, sodium and potassium (Harsh and Siddiqui, 1973). Comparatively little attention has been paid to magnesium metabolism in humans during pregnancy and most of the studies have been conducted on livestock or in experimental animals (Caddell et al, 1973). However, it is realised that maternal magnesium requirements increase during pregnancy because of increased protein synthesis and other biochemical functions related to fetal growth. In Indian fetuses the magnesium ~~content~~ appears to be considerably lower than those reported in literature. (Apte and Iyengar 1972). This might be due to the poor dietary status of the pregnant mothers. The demands of the fetus are particularly high during the last trimester because of rapid growth. A number of investigators have found maternal serum magnesium concentration to decrease significantly towards term (Hall, 1957; Lim et al, 1969; Caddell et al, 1973; Annual Report NIN, 1978). In recent years a greater emphasis is being laid on the role of magnesium than calcium in the causation of pregnancy induced hypertension (PIH) and eclampsia. It is suggested that an alteration in the Ca:Mg ratio might be responsible for the induction of PIH. (NIN Annual Report, 1984-'85). Hall (1957) showed a response to magnesium therapy (Parenteral magnesium sulphate) in toxemic pregnant women.

In spite of a fall in serum levels, high retention of magnesium was found in pregnant women (Caddell et al, 1973;

Ashe et al, 1979), but such retention may not take place if the diet is inadequate and the water is soft as in Kerala.

As mentioned earlier, calcium is one of the nutrients which is limiting in the diets consumed by the poor. The utilization of the mineral is known to be enhanced by long term adaptation to low calcium diets and during pregnancy (Nicholis and Nimalasuriyā, 1939). The apparent absorption and retention of calcium, phosphorus and magnesium are found to be increased during pregnancy and under deficient condition. (Coons and Blunt, 1939; Duckworth and Warnock, 1942; Beaton, 1961; Shinolikar, 1970). Also the improvement in calcium retention is found quite early in pregnancy when the fetal demands are low (0.15 mg/day) so that maternal stores are enriched during early pregnancy.

Iron is another mineral, the supply of which is critical during pregnancy. The iron content of the fetus at birth is found to be about 375 mg, on the basis of analysis. Iron transfer to the fetus during the last trimester of pregnancy may be as much as 4 to 7 mg/day (Toverud et al, 1950). The normal requirement for women in the child bearing age may be of the order of 2.5 mg (NIN Annual Report, 1968) so that the total requirement may be of the order of 7 mg on an additive basis. However, iron absorption is also found to be more efficient during pregnancy (Balfour et al, 1942; Hehn et al, 1951) and increases from 8 - 10% in the first trimester to

25 - 30% in late pregnancy (Apte and Iyengar, 1970). Iron absorption is dependent on the relative concentrations of transferrin, the iron-binding protein of plasma (Charley and Saltman, 1960) and the concentration of the same is found to increase with progress of gestation (Beaton, 1960; Gulyaev, 1974).

Regarding the adequacy of vitamin nutrition during pregnancy and lactation, those which appear limiting in ordinary diets are vitamins A, B₂ and C. To this list must be added folate because of the reported beneficial effects of folate supplementation during pregnancy, and also perhaps pyridoxine whose requirement is believed to be increased during pregnancy (Heller, Salkeld and Korner, 1973; Gandy and Jacobson, 1977; Dave, 1980). Paradoxically, the later two are among the vitamins whose concentrations in the milk of poor Indian women seem to compare well with those in upper class and in Western women (Deodhar and Ramakrishnan, 1960).

While the water soluble vitamins cross the placenta quite efficiently, the transport of fat-soluble vitamins seems to be relatively limited. While the fetal liver has high concentrations of the water-soluble vitamin as compared to maternal liver, this is not true of the fat soluble vitamins (Mitchell, 1964). The latter can be a protection against their possible teratogenic effects. The concentration of vitamin A and

carotenoids are lower in the fetal than in the maternal blood (Lewis et al, 1947). Hepatic stores of vitamin A are reported to be lower in a study by Iyengar and Apte (1972) than reported elsewhere ^{they} and commented that these infants may be predisposed for an early development of the deficiency of vitamin A.

Most of the stores of fat soluble vitamins seem to be acquired after birth (Arroyave et al, 1975). It is not surprising, therefore, that deficiencies of fat soluble vitamins such as vitamins D, E and K are much more common in the new born than those of water soluble vitamins. Congenital deficiency of vitamin A is rare but not unknown. However, in children in the rice eating areas, stores of vitamin A before and soon after birth may be a contributory factor in the etiology of post weaning vitamin A deficiency as milk levels are also low in such women (Srikantia, 1975).

The diets of pregnant and lactating women provide about 200 - 400 mcg of vitamin A (Shanker, 1962; Rajalakshmi and Nanavaty, 1964; Rajalakshmi and Ramakrishnan, 1969). This amount is not adequate even for the non-reproductive state. Unfortunately, rich sources of carotene such as leafy vegetables and yellow and red vegetables are not consumed in liberal amounts. It is not surprising, therefore, that symptoms of vitamin A deficiency are widely prevalent and serum vitamin A levels are low. Conflicting reports have been made of changes in the serum concentrations of vitamin A.

Serum vitamin A levels are found to fall during pregnancy and this fall was found to be prevented by supplementation of vitamin A (Lewis et al, 1947; Venkatachalam et al, 1962; Gopalan and Raghavan, 1969). Gal and Parkinson (1974) in an extensive study through pregnancy and post partum period found an initial fall in serum vitamin A and carotenoids in the first trimester ^{and} as pregnancy advanced. Towards the end of gestation vitamin A values again decreased, but rose after delivery slowly to normal levels. Prevalence of clinical symptoms of vitamin A have been observed during pregnancy and they were reversed after partus (Dave, 1980).

A number of investigators have reported a progressive increase in serum vitamin E levels during pregnancy. The levels at term are 60 - 65 per cent higher than non-pregnant levels (Varangot et al, 1943; Strauhfjord and Quaife, 1946; Vobecky et al, 1973; 1974, ^{Annu. Rep.} NIN., 1978). The rise in tocopherol is shown to be associated with an increase in the lipoprotein fractions (Dasai and Lee, 1974; Rajaram et al, 1974; Aftergood et al, 1975) which are involved in its transport. The rise in tocopherol is consistent with the general increase in many serum lipids (Davies et al, 1969; Dasai and Lee, 1974; Bieri and Ferrel, 1976).

A number of studies carried out on normal healthy populations showed a mean range of 0.7 to 1.2 mg percent of serum tocopherol (Vitamin E) and values less than 0.5 to 0.7

were considered as deficient levels (Harris et al, 1961; Bieri et al, 1964; Rehman et al, 1964; Leonard et al, 1972; Farrell et al, 1978).

Regarding the 'B' group of vitamins, folate has come in for considerable attention as it plays a key role in embryogenesis and fetal growth. Supplementation with folate is found to promote birth weights in poorly nourished women (Iyengar and Apte, 1970; Iyengar, 1971; Yusufji et al, 1973; Roopnarinsingh et al, 1976; Gandy and Jacobson, 1977). Pyridoxine has also aroused interest because of the increased excretion of xanthurenic acid (Wachstein and Gudaitis, 1952, 1953) attributed to a deficiency of this vitamin during pregnancy. Animal studies suggest that an adequate supply of the 'B' vitamins particularly of pantothenate may be more critical in early gestation associated with organogenesis than during the subsequent stages, associated with fetal growth (Nelson et al, 1957; Mitchell, 1964). Recently it has been pointed out by Schorah et al (1983) that mothers who are prone to give birth to babies with neural tube defects, supplementation with generous doses of 'B' vitamins will reduce the risk appreciably.

Many of these changes such as those with regard to blood hemoglobin, serum vitamin A, folate and xanthuremic acid are found to be partly or fully reversed after delivery (Rajalakshmi and Ramakrishnan, 1969; Dave, 1980).

Factors influencing gestation performance and birth weights:

Studies on gestational performance of women subjected to acute food shortages could be possible during famine, especially in war time Europe or chronic starvation as in poor segments of the world's population.

During the long siege of Leningrad (1941-42) when conditions were reported to be particularly severe (Antonov, 1947), birth weights fell by a maximum of 600 g. During the Dutch famine of 1945, most Rotterdam women gained only about 2 kg during pregnancy and many lost weight and yet the average birth weight fell by only about 240 g with little or no effect on neonatal mortality. However, the above studies refer to periods of acute and severe shortages in foods in population groups who were well nourished prior to such extreme stress. The question arises as to what happens with chronic under-nutrition and malnutrition aggravated during pregnancy.

Many of the early studies point to a positive relation between the adequacy of maternal diet and the outcome of pregnancy. Bruke and his associates found that incidence of still-birth, neonatal deaths, prematurity and congenital abnormalities to be higher in the poorly nourished group (Bruke et al, 1943a). In contrast almost all the infants born to well nourished mothers were found to be in good physical condition at birth. Obstetric

performance however was also less satisfactory in the poorly nourished mothers and the infants born to these mothers were smaller at birth. Similar findings on the relation between the adequacy of maternal diet and economic condition, on the incidence of still births, prematurity, small-for-date and neonatal mortality have been reported by a number of investigators (Graham, 1944; Moneriet, 1948; Gopalan, 1949; Varkki et al, 1955; Thomson, 1959b; Arora et al, 1962, 1963; Aldrich, 1965; Woodruff, 1965; Nirmala et al, 1966; Rajalakshmi and Ramakrishnan, 1969; Srivastava et al, 1976; Prentice et al, 1983, 1987; Kennedy and Kotelchewik, 1984; Matcoff et al, 1985; Brown, 1986).

On the other hand, several studies including those carried out in this laboratory suggest a reasonably satisfactory gestation and obstetric performance of women on a low plane of nutrition on the whole, as judged by mean birth weights, duration of labour, toxemia of pregnancy, obstetric complications etc. (Williams and Fralin, 1942; Woodhill et al, 1955; McGanity et al, 1954; 1955; Thomson, 1959; Rajalakshmi and Ramakrishnan, 1969; Srikanthia and Iyengar, 1972; Rajalakshmi, 1977). However, the average performance marks the fact that other indices such as low birth weights, prematurity, still births and neonatal mortality show them at a disadvantage (Rajalakshmi and Ramakrishnan, 1969; Bhatt et al, 1969; Aiyar, 1972; Parekh, Naik and Udani, 1972; Banik and

Saha, 1975; Ghosh et al, 1977; Banik, 1978; Purohit, 1979).

In this country, mean birth weights are of the order of 2.7 kg in the low income group, and 3.0 kg in the high income group. But even a small difference of this order in mean birth weights may signify appreciable differences in the proportion of low birth weight infants as can be seen from the data on low and high income groups in this country (Table - 3).

Increase in protein and calorie has been claimed to be beneficial in some cases against miscarriages and premature births and still births (Strauss, 1935; Ebbs et al, 1941; Ebbs and Moyle, 1942a; Ebbs et al, 1942b; Stuart, 1947; Arora et al, 1963; Srikantia and Tyengar, 1972).

On the other hand, in several studies, no association was found between protein intake and birth weights and other parameters (Huggett, 1944; Pasricha, 1958; Crump et al, 1959; Kennedy and Kotelchwk, 1984; Metc~~off~~et al (1985). Prentice (1985; 1987) found a small but positive effect on birth weights with supplementary feeding in the WIC programme.

TABLE 3: Distribution of birth weights in lower and upper classes

	Rajalakshmi (1971)		Udani (1963)		Achar and Yankauar (1962)	
	HIG	LIG	HIG	LIG	HIG	LIG
No. of subjects	81	820	270	1000	256	235
Birth weights (Kg):						
3.5 and above	11	6	15	5	18	3
3.0 - 3.5	30	16	31	18	35	18
2.5 - 3.0	39	39	33	34	39	45
2.0 - 2.5	20	29	16	29	9	26
1.6 - 2.0	0	10	5	14	2	8

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Per cent of subjects

HIG - High income group
LIG - Low income group.

The major nutritional interventions during pregnancy include food energy and protein (Venkatachalam, 1962; Srikantia and Iyengar, 1972; Qureshi et al, 1973; Habichet et al, 1974; Iyengar, 1975; Mora et al, 1979; Agarwal et al, 1984), Iron and folate (Iyengar and Apte, 1970; Iyengar, 1971; Srikantia and Iyengar, 1972; Gandy and Jacobson, 1977) and the major outcome is found to be the promotion of birth weights.

Inspite of efficient conservation and utilisation of iron during pregnancy, anemia is a major problem encountered in gynecological practice, hemoglobin levels below 5 g% being by no means a rarity (NIN, Annual Report, 1980). Severe anemia is also responsible to a large extent for maternal mortality and morbidity in poorer areas and more so in the case of preterm infants because of placental hypoxia (Reinhardt, 1978). Levels below 10 g/dl in pregnancy are taken to signify anemia (Darby et al, 1963). Such levels were encountered only in 10.3% of the pregnant women in the well known Vanderbilt co-operative study as against around 50% in late last trimester of pregnancy in India and elsewhere (Rajalakshmi and Ramakrishnan, 1969; Gopalan and Raghavan, 1969; Subbalakshmi, 1970; Yusufji et al, 1973; Scott, Goldie and Hay, 1975; Adams and Gurung, 1977; Garn et al, 1977; Hussain et al, 1977).

Maternal hypoferremia and/anemia is associated with reduced iron content in placenta and cord blood and at term,

fetal and neonatal liver stores are also significantly reduced (Bhatt et al, 1969; Cavill et al, 1977; Singh and Sindhu, 1979; Singh et al, 1980). The onset of anemia of infancy is more rapid in Indian infants, particularly in those born of anemic mothers and the rise of hemoglobin to adult values following weaning age is very slow and is associated with the outcome of anemia (Rosario, 1971; Agarwal, 1984), the resultant effect of this being more premature deliveries and fetal and maternal deaths.

A fall in folate levels during pregnancy has been reported (Rajalakshmi and Ramakrishnan, 1969; Yusufji et al, 1973; Colman et al, 1974; Roopnars^{ING}ingh et al, 1976).

Treatment with a single large dose of iron in the last trimester significantly improved fetal weights and reduced placental shrinkage, though the histological changes found with placental aging were not reversed (Agarwal et al, 1981). However, a rise was found in iron supplementation (Agarwal et al, 1981). Studies in Hyderabad (Srikantia and Iyengar, 1972; NIN Annual Report, 1974, 1984-85) suggest that supplementation during pregnancy of 60 mg iron and 300-500 mg of folic acid and 2 mcg of vitamin B₁₂ help in preventing severe anemias and low birth weights. Also 100 mg of elemental iron in intra-muscular therapy daily for 10 days for those with hemoglobin levels $\leq 8\text{g/dl}$ (NIN. Ann. Rep. 1981) and 200 mg daily

intra-muscular iron therapy for 5 days (NIN. Ann. Rep., 1984-85) suggest that the later practice might prove to be an effective strategy in avoiding discontinuation of therapy and in improving the hemoglobin levels of pregnant women as well as in increasing the birth weight of the infant.

Inadequate supplies of the fat soluble vitamins specially vitamin A and E in pregnant women are reported to lead the progeny to growth retardation (Baker et al, 1977; Brandt et al, 1978; Shenai et al, 1981; Shat et al, 1984; 1987). Thus it is suggested that vitamin A and E are to be considered as critical nutrients in the prevention of low birth weights and premature births.

Adair et al (1984), Adair and Pollitt (1985), Brown et al (1986) and Prentice et al (1987) from their studies summarised that supplemental feeding programmes to pregnant women sometimes may not show the needed beneficial effects on the mothers status and sometimes may even show low increments in birth weights because of some important mediators which include sex of the off-spring season of birth, maternal body size, birth of the previous infants characterised by dysmorphic prenatal growth, educational status and age of the mother, and the time of the day at which the supplement is offered to the mother. Therefore in supplementing the at risk pregnant women these critical factors must be considered. However the

reduction in infant mortality rate, low birth weight babies, and premature births can support the notion that the infant can still benefit from maternal supplements. It is also stated that the limited effect of supplementation on the population as a whole may reflect the operation of a long term adaptation which allow women to maintain reproductive success despite their apparent marginal status.

It has thus been shown that even in the low income group a reasonable weight gain is achieved normally during pregnancy which can be compared with that in the high income group. However, in a certain proportion of poor women, weight gains may be too small to permit normal placental and fetal growth on the basis of the association found previously between birth weight and weight gain in this laboratory (Rajalakshmi and Ramakrishnan, 1969; Rajalakshmi et al, 1978) and in other laboratories (Eastman and Jackson, 1968; Duffus et al, 1971; Munro, 1973; Desai et al, 1974; Sen and Agarwal, 1975; 1976; Stein et al, 1975; Rosso and Chamog, 1979; Metcoff, 1980; 1981; 1981a; Woods et al, 1980).

The capacity of poor women to adapt to low plane of nutrition and the failure of this adaptation when nutrient supplies are below critical levels, have been commented on by Rajalakshmi and Ramakrishnan (1969); Rajalakshmi (1971), Lechtig et al, (1975) and Metcoff (1982).

In some studies, maternal weights and birth weights are also shown to be correlated (Douglas and Scadron, 1951; McKoewan and Record, 1957; Thomson and Billewicz, 1957; Williams, 1957; Stewart and Howitt, 1960; Clements, 1961; Emerson, 1962; Kaltreider, 1963). In a recent study Bhatia et al, 1983) also showed a relation between fetal size and weight for height ratio of the mother. This was not found to be the case in studies of Hillman and Hall (1964). However, weight gain of the mother during pregnancy rather than pre-pregnancy weight seem to be more critical.

Thus, fetal growth seems to be determined by a number of factors and it is only recently that biochemical indices which change during pregnancy such as plasma volume blood glucose, serum lipids vitamin deficiencies and other constituents and the correlations between these indices and the outcome of pregnancy have engaged the attention of at least a few scientists who made attempts to determine the relative contribution of these different factors. In fact, studies suggest that using these various indices at mid-pregnancy, it is possible to predict the risk indicators of maternal malnutrition and the outcome of pregnancy and use appropriate interventional measures wherever needed (Metcoff, 1974, 1982; Iyengar, 1982, 1985; Shah et al, 1984, 1987).

Thus pregnancy is seen to be associated with an increase in serum lipids and body fat satisfactory intake of food energy with an adequate proportion derived from fat may be critical. The increase in cholesterol is critical for the steroid hormones which increase during pregnancy and play a critical role. Similarly the elevation of serum triglycerides is perhaps critical for fat deposition and the growth of accessory tissues, not to mention the need for the transfer of fatty acids, particularly, essential fatty acids to the fetus. A question arises as to whether the expected increases in serum lipids are achieved in poor pregnant women and what are the consequences of failure to do so.

A similar question arises regarding magnesium status during pregnancy as serum levels tend to fall during pregnancy. The question arises as to the adequacy of magnesium status during pregnancy in an area such as Kerala, where the diets are marginal with regard to magnesium.

The present investigations were thus designed to carry out studies on serum lipids (cholesterol, phospholipid and triglyceride) and magnesium in pregnant and parturient women in relation to the period of gestation in the former and gestational age and birth weight of infant in the later. Additional investigations were made on serum vitamin E and blood hemoglobin.

Some of the changes which take place during pregnancy such as rise in serum lipids are also found with aging. While in the former case the changes are conducive to satisfactory gestational performance, this is not the case in the elderly and may lead to obesity, hyperlipidemia and other degenerative diseases. Thus studies were carried out on adults to see the aging changes on selected parameters as mentioned earlier.

SECTION II: Aging Changes in Relation to Diet

Malnutrition in early life which looms large on the horizon in the poor segments of the world's population, and its etiology, prevalence, consequences, prevention and alleviation, have aroused the concern of nutritionists, social workers and administrators throughout the world, although belatedly. But with the advent of affluence in the privileged segments of the world's population, other problems have begun to manifest themselves. Affluence has lead to altered life styles associated with an appreciable reduction in physical activity, replacement of cultural traditions such as a balance between fasts and feasts by chronic feasting increasing the consumption of foods of doubtful nutritional value with high energy content such as refined sugars and fats, and of non-food items such as coffee, tea, alcohol and tobacco. These changes have been associated with increased prevalence of obesity, diabetes mellitus, hypercholesterolemia, hypertension, cardiovascular disorders and cancer of the blood and intestine (Trowell, 1972; Burkitt et al., 1974; Rockstein and Sussman, 1976).

With progressive deterioration in physiological (Gussek, 1972; Timiras, 1972; Andres and Tobin, 1976) and neural (Timiras, 1972) regulation, an age dependent decline is found with regard to resistance to radiation (Storer, 1965;

Kohn, 1971), cold stress and other physiological (Kohn, 1971; Timiras, 1972) and emotional stresses (Kimmel, 1974).

It is also a mute question as to what extent such consequences are due to current life styles, and to what extent they are due to the long term effects of dietary patterns from early life. At least some studies indicate a correlation between diet during childhood and proneness to hypertension in later life and between obesity in childhood and maturity (Brozek et al., 1953; Mayer et al., 1968).

Although life span in the affluent areas of the world is greater than that in poorer areas, disorders such as cardiovascular diseases and cancers of the gastrointestinal tract claim a major share of adult mortality in affluent areas. This raises questions regarding the process of aging and how some of the diseases of the type mentioned above could influence this process. In addition, during adulthood important changes occur in the body composition (Fig. 1) including a progressive increase in body fat and a decrease in lean body mass (Frobes and Reina, 1970). The process of demineralization is a general phenomenon more marked in women than in men. Similar changes are seen with age with regard to body weight, blood pressure, physical activity and other indices. These changes during ontogeny are sought to be explained in terms of theories regarding cell cycles, the capacity for cell renewal,

the balance between anabolic and catabolic processes, and tissue turnover rates which result in increased endogenous losses of nutrients (Shock *et al*, 1963). However, the tendency was to accept these as inevitable alterations in various components during the aging process

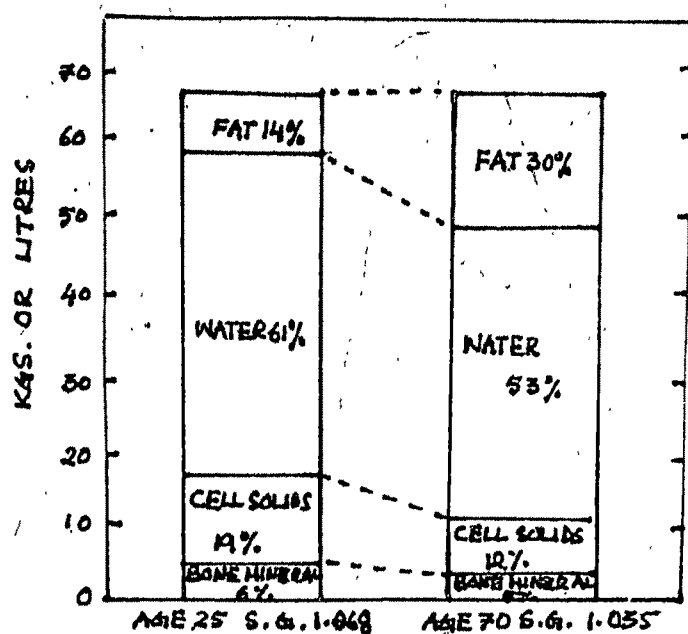


FIGURE 1: Body composition in young and old age.

Weight, height and somatic changes in the elderly:

It has long been known that during adulthood important changes in body composition take place such as a progressive increase in body fat, decrease in lean body mass with alterations in skeletal weight (Frobes and Reina, 1970).

In addition, the nature and magnitude of age specific changes may vary with the plane of nutrition. Some changes

such as increase in body weight, blood pressure, blood glucose levels, hyperlipidemia etc. (Tanner, 1962, 1966, 1968, 1978; Bakwin, 1964; Milev and Demireva, 1966; Roberts and Dann, 1967; Zacharias et al., 1970; Harper and Collins, 1972) seem to be less evident among the poor who are generally undernourished than in the affluent sections of the population with luxury intakes. However, these changes are becoming increasingly evident in developing countries with a growing urban elite with altered life styles. For instance, periodic fasting followed by feasts has been replaced by luxury consumption. But, more striking phenomenon is the increase in body weight and its continued increase with ages after adult stature is reached in overnourished individuals. Studies on weight changes in the aged have been reported by a number of investigators (Rao, et al., ICMR, 1961; Stoudt, et al., 1965; Milev and Demireva, 1966; Parot, 1966p;; Rajalakshmi and Chandrasekhar, 1966; Underwood et al., 1972; Watson and Etta, 1975; Angelico et al., 1976 Albrink and Meigs, 1977); Rossman 1977). The progressive increase in body weight is associated with obesity and hyperlipidemia (McDonand, 1964, 1965; Knittle, 1971)

On the contrary, height tends to decline with advancing age. Longitudinal studies indicated more variability in the onset and extent of decline in stature. The tendency to diminish in height with increasing age is more clearly marked in men than in women. Buchi (1950) found a

decrease in height to occur during the fourth decade in males. The decrease began at about the age of 47 years and amounted to 2.9 cm in those past 70 years. However, an overall decrease of 3 - 10 cm around 70 years in height is reported by different investigators (Pett and Ogilvie, 1956; Rao et al., 1961; Stoudt, 1965; Milev and Demieriva, 1966; Howells, 1970; Rossman, 1977).

The decrement in height is interpreted by different investigators in different ways. Stoudt et al (1965) reported that the 'slump' in height might be due to increased spinal rigidity, while Howells (1970) reported it to be due to postural habits as the older individuals carry themselves with a flexion at the knees and hips. In areas where investigators reported an increase in height (Buchi, 1950; Gsell, 1967), Buchi himself interpreted that it might be due to swelling in the intervertebral discs or an enlargement of the individual vertebrae as reported by Isreal (1973a). These phenomena are associated with diminished intervertebral disc space and consequently, with decrements in height.

The accumulation of fat under the skin generally grows progressively with advancing age reaching a peak at about 40 years of age for men and between 40 and 60 years for women, after which the trend is reversed with a fall to the levels found in the young adult. Skinfold thickness also progressively

increases. However, in some instances, subcutaneous fat in the arm may show little of the increase because of fat deposition elsewhere, e.g. abdomen or thighs and hips. These changes are highly variable and may not be found in all population groups not to mention intra-group variations. Albrink and Meigs (1971) showed little weight gain or increase in skinfold thickness with aging in the subjects he studied.

Similar observations have been made on poorly nourished indigent male population described by Lee and Laskar (1958). In the typical economic circumstances of Western society, skinfold measurements increase with aging falling off only in the 7th or 8th decades, but with marked differences between males and females (Pett and Ogilvies, 1956; Stoudt, et al, 1970). Ryckewsert, et al (1967) emphasized the value of measurements of the subcutaneous skinfold of the back of hand. This measurement decreased rapidly after 45 in the female though weight continues to rise; the decrement occurs later in males.

With both sexes, subcutaneous fat accumulates at the fastest rate and attains the highest values in the back. The arm data shows the greatest difference between the two sexes with regard to the nature of the curves as well as the absolute degree. With men, skinfold changes vary slightly during their

life course and has the lower values, while with women it is extremely dynamic inspite of its considerably higher initial level. In men, the fat accumulation is very dynamic in the back and abdomen. The skinfold measurements at the chest registers the smallest differences between the two sexes (Milev and Demireva, 1966).

Most of the skinfolds in women tend to remain stationary until around age 65. The females could be characterized as showing a greater deposition of fat and a longer maintenance of the thickness of fatty depots. Of the variations in skinfold measurements the humeral (triceps), paraumbelical and dorsal skinfold of the hand have been singled out by Bourliers (1970) as best correlated with aging.

Chest changes were not considered seriously during aging changes. However, it seems clear that the chest undergoes an increase in size with aging. Among the Irish males the chest diameter kept rising to a peak of about 30 cm, average at 50 - 54 with slight deminution in the decades thereafter to 29.25 cm in the 75 - 79 year. However, this was followed by a terminal rise to 30.15 in the above 80 years of age. It seems clear that an anteroposterior diameter of the chest is characteristic of aging and over-rides secular trends.

Recently Frisancho and Flegel (1983) and Frisancho (1984) suggested the use of elbow breadth to assess the nutritional status of the elderly as it is less affected by degree of adiposity than other anthropometric dimensions and also because it measures skeletal breadth it can be used as an indicator of frame size as well.

The various morphological and anthropometric changes suggest that body composition must undergo major changes with aging. Increase in skinfold and decrease in muscle mass suggest that water, fat and mineral changes are to be anticipated. It has long been known that the organs of healthy older people are smaller than the younger age group (Rossle and Roulet, 1932; Calloway et al., 1965).

Blood glucose in the elderly:

Blood glucose is another parameter which tends to increase with age in certain population groups. Interest in this problem arose from epidemiological observations on the prevalence of diabetes in different groups in a state of transition which revealed a ten-fold increase in the prevalence of diabetes as dietary habits have changes from a primitive to a more refined, western type diet (Cohen, 1961; Campbell, 1963; Jackson, 1976; Prior et al., 1978; West 1978). However, these studies have been carried out on subjects above 50 years of

age and no comparisons have been made with young adults.

Strong arguments have been made for increased dietary sugar and/or refined starch intake as a contributor to the increased incidence of diabetes and to effect several indices of glucose tolerance (Cohen et al., 1972a; Cleave, 1974; Reiser et al., 1981). However, others feel that sucrose does not correlate with increased risk for diabetes. Manoz et al. (1978) and Jenkin et al. (1978) suggested that complex carbohydrates in the diet improve glucose tolerance and prevent diabetes and that high dietary fat intake is a risk factor for diabetes. A decrease of total fat intake is now recommended in the treatment of diabetes mellitus, Arky et al. (1982). Trowell (1975, 1978) has suggested that the very low crude fibre content of western style diet contributes to the etiology of diabetes. Calorie density of the diet is related to obesity, and possibly to diabetes as well. It should be pointed out that risk factors associated with diabetes are obesity, excessive calorie intake and composition of the diet.

There is little doubt that the life expectancy of the diabetic subjects is less than that of the non-diabetic one primarily due to premature vascular disease (Marks, 1965).

As mentioned earlier, fasting blood sugar levels and glucose intolerance increase with age (O'Sullivan, 1974) but

it is not clear if this glucose intolerance correlates with the capillary thickening of basement membrane. It has been shown that in diabetes capillary basement membrane thickness at a faster rate. The thickness of the basement membrane in 20 year old diabetic is similar in thickness to that of 40 to 50 years old non-diabetic.

Careful regulation of calorie intake and composition of the diet helps to normalize the metabolism of the diabetic and prevents complications of diabetes (Stone, 1961; West, 1973).

The proneness to diabetes mellitus after middle age among the effluents is well known. Comparative glucose tolerance curves of the older and youngmen showed that the average blood glucose levels of the older men were higher than those of the young men at comparable times (Horwitt, 1953). On the other hand, Gillum et al, (1955) who studied on old men in age range 50 years to above 70 years found no differences with regard to mean blood glucose levels. This might be because the comparison was made between the middle aged and the old but not between the young and the old.

It is now realized that blood glucose levels may not necessarily be affected by age but that they show a tendency to rise with certain types of diets and life styles. Silverstone et al (1957) found diminished glucose tolerance

in the elderly and interpreted it to be a common finding, ^{and} Silverstone et al., (1957), Gupta et al. (1978); Verma et al., (1986) showed that income status and even urban rural environments have a role to play on the incidence of type II diabetes. Scholfield et al. (1987) showed a racial predisposition to glucose intolerance.

Serum Lipid Changes in the Elderly:

Most of the emphasis with regard to dietary lipids was on cholesterol and the quantity and quality of dietary fat, although some consideration is now being given to other dietary constituents such as amounts and type of carbohydrates including fibre quality and protein, trace elements, coffee, tea and several other factors such as exercise and smoking habits.

Hyperlipidemia is manifested with regard to all the major components of the serum, namely, total fats and fatty acids, triacylglycerol (triglycerides), phospholipid and cholesterol and tends to be associated with lipid deposits on the walls of blood vessels.

Epidemiological surveys on the pathogenesis of atherosclerosis and other related diseases due to hyperlipidemia lead to a number of intriguing factors to decide over the normal cholesterol levels in serum. This has been borne

out by reports from many areas of the world demonstrating a wide variation in the normal cholesterol levels. A number of studies showed that serum cholesterol may vary in relation to age, sex, race, nationality, socio-economic condition and most important, the diet.()

a. Role of age, sex and environmental factors on serum lipids:

A number of workers studied the serum cholesterol levels at different ages. In an extensive study, Werner and Sareen (1978) observed that the serum cholesterol levels increased gradually after the age twenty. The greatest rate of increase of serum cholesterol in males occurs from the age of 20 and reaches the peak around 45 years. The curve then assumes a broad curvilinear configuration showing small increases upto 60 years followed by a plateau or decrease.

It is observed that in female the serum cholesterol is lower in comparison to males upto the age of 45 to 50 years and then rises up continuously showing greater differences between sexes (Barker, 1939; Turner et al 1939; Kornerup, 1950; Gillum et al, 1955; Keys et al., 1957; Feldman et al, 1963; Schilling et al., 1964; Schaefer 1964; Nicholas et al, 1976; Werner and Sareen, 1978). In a recent study by Berry et al (1986) on stepwise regression showed a high correlation between serum cholesterol, LDL-C and age.

An essentially similar pattern is found with regard to serum triglycerides (Carlson, 1960; Albrink et al., 1962; Schaefer, 1964; Schilling et al., 1964) and phospholipids (Barker, 1939; Kornerup, 1950; Carlson, 1960; Berry et al., 1986). The proportions of the three major lipid components do not seem to show appreciable changes with age (Kornerup, 1950). Serum phospholipid changes are closely parallel to serum cholesterol (Ahrens et al., 1954; Grande et al., 1972).

High levels of serum cholesterol are more prevalent in post-menopausal women. Serum triglyceride levels are lower in women during 24 - 40 years of age and rise thereafter. This phenomenon of rise is not found in men of reproductive age group. This suggests the operation of a factor which regulates serum lipid levels in women in this age group. This suggestion is reinforced by the finding in oophorectomised women and those who underwent hysterectomy. The protection against early hyperlipemia and fatty streaks in the aorta with delayed atherogenesis is also attributed to a genuine sex difference due to factors other than ovarian functions (Keys, 1973) because of built in differences in genetic characteristics.

A significant correlation has been observed with certain other parameters such as body measurements and serum lipids (Albrink et al., 1962; Feldman et al., 1963;

Albrink and Meigs, 1964, 1971; Panjer and Harrison, 1982) but Schilling et al., (1964) failed to find such an association.

A number of studies have shown that serum cholesterol levels change (either increase or decrease) with environmental factors, and social, religious and cultural practices (Walker and Arvindson, 1954; Mendoz et al., 1959; McCullogh and Lewis, 1960; Schilling et al., 1964; Malhotra, 1967; Werner and Sareen, 1978; Singh et al., 1980; Gandhi, 1982).

The relationship between the different dietary factors such as type, quality and quantity of fat, carbohydrates, proteins etc., with serum cholesterol and triglycerides has been studied extensively and are summarized below.

Role of dietary fat on serum lipids

The relationship between serum lipids and high fat diets and their role in heart diseases, increased blood pressure and atherosclerosis have been well documented. (Report of the AHA Nutrition Committee 1982 (Williams et al., 1986)

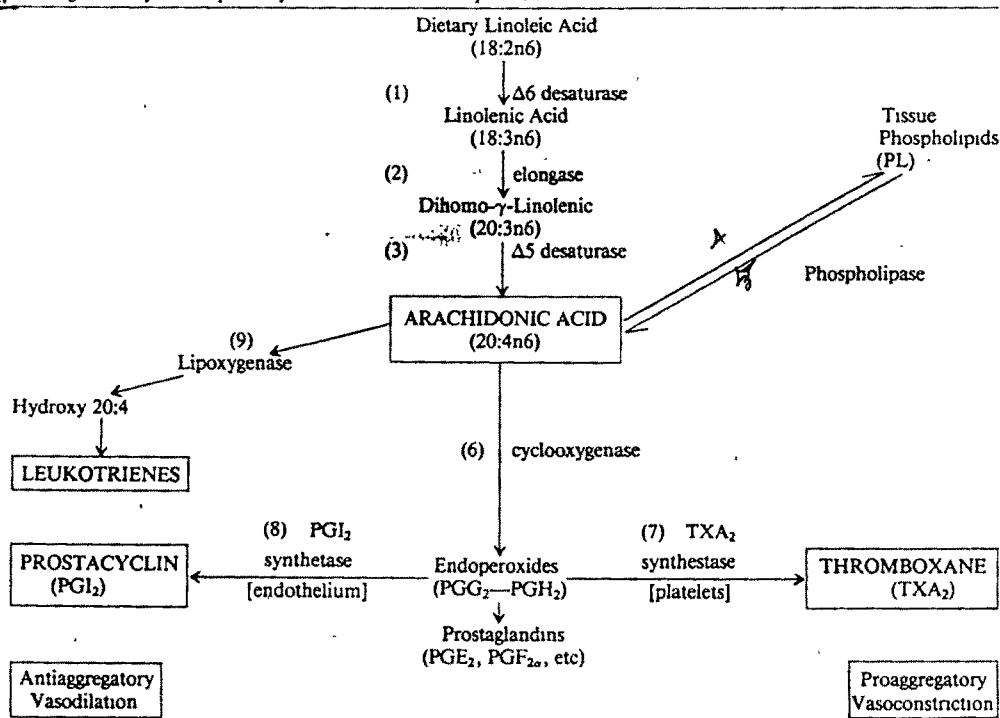
Many investigators found that in populations consuming low fat diets, the serum cholesterol levels are low and the people are devoid of the diseases due to hyperlipidemia (Bose and De, 1936; Keys et al., 1954; Bronte et al.,

1955; Keys et al., 1955; Gillum et al., 1955; Walker and Arvidson, 1954; Keys et al., 1958; McCullagh and Lewis, 1960; Keys 1975; Stemmler 1979; Glueck 1979). However, this view was questioned by Murray et al. (1978); Werner et al. (1978) on the basis of their studies on populations who had low serum cholesterol levels in spite of consumption of diets high in fat content. The non-elevation of serum lipids with high fat intake in some groups raised questions as to the factors that are involved in raising lipid levels in serum. It has been suggested by some investigators that it is the quality of fat rather than quantity that is critical in elevating serum lipid levels (Gillum et al., 1955; Morris et al., 1963; Fidenza, 1969; Easty, 1970). Thus the role of vegetable oils containing poly-unsaturated fatty acids (PUFA), specifically, oils such as corn oil containing linoleic acid, an essential fatty acid (EFA) in lowering serum cholesterol levels, came into light (Aherens et al., 1957; Siato et al., 1965; Grande et al., 1972). However, coconut oil though a vegetable oil shows an increase in serum cholesterol because of the higher proportion of saturated fatty acids present in it (McGandy et al., 1966). Fats of animal origin such as lard and butter also contain saturated fatty acids and their consumption is associated with an increase in serum cholesterol while fish and fish oils though of animal origin decrease serum cholesterol because of high amounts of PUFA of the type ω -3 and ω -6 fatty acids.

Thus in areas where marine foods and oils are consumed serum levels of cholesterol, triglycerides and VLDL, LDL and HDL are reported to be lower (Imaichi *et al.*, 1953; Ahrens *et al.*, 1959; Kingsbury *et al.*, 1961; Nelson, 1972; Lossonczy *et al.*, 1978; Lonnor 1986; Nestel 1986; Herold and Kinsel 1986, *Nutr. Reviews* 1986). A low fat and high P/S ratio are thus used in lowering cholesterol to reduce blood pressure and atherogenesis (Iacono *et al.*, 1983).

Studies have provided evidence that marine oil has detectable antithrombotic and hypolipidemic effects because of the Eicosapentaenoic acid (EPA 20:5n-3) and docosahexaenoic acid (DHA 22:6n-3). The role of PUFA in reducing cardiovascular diseases by the formation of prostaglandins and prostacycline and aversion of platelet aggregation. The mechanism of action is summarised in table - 4.

Table 4. Prostaglandin synthetic pathways in blood vessels and platelets*



* The scheme shows the key sites in conversion of dietary linoleic acid to arachidonic acid and then to prostanoids and leukotrienes. The key enzymatic steps likely to be affected by dietary n-3 polyunsaturated fatty acids are 1 and 6

One of the lipid components, cholesterol, is widely distributed in animal foods which is in itself a causative factor to increase serum lipids/or cholesterol. However individuals vary in their response to dietary cholesterol. Individuals with higher serum cholesterol levels show a greater response to change in their dietary fat or cholesterol than those with lower levels. However it is agreed that whatever be the response for dietary cholesterol the response does tend to plateau at some level of intake. Serum cholesterol appears to be linearly correlated to dietary cholesterol. For every 100 mg of dietary cholesterol per 1000 kilocalories in the diet an increase of 5-12 mg is reported (Gillum et al., 1955; Hegstead et al., 1965; Mattson et al., 1972). In a recent article Hegstead (1986) showed that with a 2500 Kcal diet an increase in intake of 190 mg/day of cholesterol would be expected to increase serum cholesterol by 4 mg/dl. Neutral fat augments this effect by facilitating absorption. Thus diets with a low amount of neutral fat may be associated with low serum cholesterol levels even when they are rich in cholesterol.

In conclusion, however, it is found that the lipid increase or decrease in different tissues, depends not only on the nature, quality and quantity of the fat consumed but also on the sex, age and life style of subjects studied. The triglycerides seem to be particularly responsive to dietary

changes (Grande et al., 1972; Nestel and Barter, 1973).

Dietary carbohydrates and serum lipids

Carbohydrates comprise of simple sugars, complex starches and non-nutritional complex carbohydrates, such as fibre, pectin etc.

Among the different types of hyperlipidemia, carbohydrate induced varieties are relatively common and are frequently found in association with clinical atherosclerosis (Gofman et al., 1954; Carlson, 1960; Antoni and Bersohn, 1961).

A number of investigators have carried out studies on the effect of different sugars (glucose, fructose, sucrose and lactose) on fasting serum cholesterol and triglyceride levels. It is found that in the normolipemic individuals, these sugars when isocalorically exchanged (at approximately 30% of the caloric intake) produced no significant elevation of serum cholesterol (Anderson et al., 1963; Sharma and Khaldi, 1963; McDonald, 1966).

However, diets rich in complex carbohydrates have long been known to cause low serum cholesterol concentrations (Starke, 1950; Stare, 1967). A significant lowering of blood

lipids was observed with isocaloric substitution of starch for sugar (Antar and Ohlson, 1965; Hodges and Krehl, 1965; Hodges et al., 1967; Kaufmann et al., 1967; Kaur et al., 1967). High sugar diets temporarily increase the serum cholesterol and triglyceride levels (Rath et al., 1973). Most of the authors agree that all carbohydrates do not act in the same way and that feeding sucrose raises the triglyceride levels more than an equivalent amount of starch.

In developing countries people derive 75% of their daily energy as starchy foods. The adult intake of crude fibre from starch sources in these countries is about 10-15g. On the other hand, in western countries 30% of their daily energy needs is met from starchy foods in the form of wheat flour, mostly refined or polished rice, and the average intake of crude fibre in these countries is about 1.0 to 1.5g/day.

A low intake of fibre has been implicated in the development of various diseases associated with urbanisation affluence and changes in life styles (Trowell, 1972; Carlson and Bottiger 1972; Burkitt et al., 1974; Walker, 1976; Trowell, 1978).

Crude fibre consists of cellulose, pectins, gums mucileges, lignins etc. when fed singly, celluloses were not

found effective in lowering serum cholesterol (Shurpulakar, 1972). Whereas pectins are found to be more effective. (Keys et al., 1961; Jenkin et al., 1975; Durrington et al., 1976; Gormley et al., 1977; Kay and Truswell, 1977; Stasse-Wolthuis et al., 1979). However, pectins had no effect on serum triglyceride (Behall et al., 1979; Robertson et al., 1979). Guar-gum from cluster beans and bengal gram have also been shown to have hypocholesterolemic effect (Mathur et al., 1968; Jenkin et al., 1975).

The effects of cereal fibres, especially wheat fibre is a matter of controversy. Truswell and Keys (1976) showed no effect of wheat fibre on serum cholesterol. These differences in the effect of different fibres might be due to the amounts of fats, carbohydrates and cholesterol in the diet or may be due to differences in the type and amount of fibres. When a high carbohydrate diet is coupled with a diet containing high fibre, the anticipated rise in fasting serum lipids (triglyceride especially) does not occur (Albrink et al., 1979). Kirby et al., (1981) and Williams et al. (1986) observed a negative relationship between plasma smaller LDL cholesterol particles and dietary (soluble) fiber intake.

These are attributed to gel formation, water holding capacity, matrix formation, bile acid absorption, cation exchange and antioxidant activities of various components of crude fibre.

Effect of plant and animal proteins on serum lipids

Several workers have reported on the basis of epidemiological surveys a positive correlation between per capita intake of total calories, fat and protein and mortality due to coronary heart diseases (Keys, 1953; Yerushalmy et al., 1957; Uwdkin, 1958; Jelliffe et al., 1959). Though other factors are also known to be involved in hypercholesterolemia and atherogenesis, most of the emphasis has been laid on dietary fat and cholesterol. Some consideration has been given to other dietary constituents such as sugar and fibre, but not much attention has been paid to dietary protein (Carroll, 1978).

Proteins derived from animal sources have a greater tendency to elevate plasma cholesterol than proteins derived from plant sources (Beveridge et al., 1959; Walker et al., 1960; Beveridge et al., 1961; Mathur et al., 1968; Behall et al., 1978; Williams et al., 1986; Park et al., 1987). This has been interpreted to be due to increased levels of very low and low density lipoprotein cholesterol (Terpstra et al., 1982, 1983). Campbell et al. (1965) substituted wheat gluten for a casein-lactalbumin mixture as the chief source of nitrogen and found no significant changes on serum cholesterol total lipid, sterol ester, glycerides, phospholipids and unestrified fatty acids. However, most of these studies are based on purified proteins

which may have a different effect when consumed in the form in which they are present in foods.

It is also to be noted that plant and animal foods contain the triglycerides which may have a variable influence on serum lipids (Kinsell et al., 1952; Bronte-Stewart et al., 1956) because of differences in their fatty acid composition and plasma cholesterol changes in response to dietary proteins (Beveridge et al., 1963). This seem to vary in men and women, the response being less in men.

The increase in serum cholesterol level with animal protein has been attributed to several factors. The availability of amino acids in the two diets, might affect amino acid utilization. Though the total dietary protein content of both diets may be the same, the effect on cholesterol mobilization is poor in vegetable proteins diet. Here the amino acid composition of the food plays a role (Park and Lipa, 1982).

Animal proteins correlate positively with concentrations of total cholesterol, triglycerides VLDL cholesterol, smaller LDL mass and VLDL mass while plant proteins appear to be inversely related to triglycerides, smaller LDL-mass and both the cholesterol content and the total mass of VLDL particles. It has also been shown that serum concentrations

of smaller LDL increase linearly as the proportion of total calories from animal protein is increased (Williams et al., 1986).

Foods with cholesterol lowering effects

It is now generally recognised that elevated serum cholesterol contributes significantly to the genesis or progression of hypertension, atherosclerosis etc. in man, and that changes in blood coagulation mechanism are involved in the development of thrombosis and atherosclerotic vessels. Numerous efforts have been made to reduce serum cholesterol and fibrinolytic activity in the treatment of hyper-cholesterolemia and cardiovascular diseases. Various substances that were reported to be of value include nicotinic acid, thyroid analogues, sitosterol, estrogens, onion, exchange resins, EDTA, androsteron, vanadium, and salicylates (Gupta et al., 1966).

It has been found that administration of garlic and onion can prevent alimentary lipemia (Jain, 1973) and also increase fibrinolytic activity. Garlic is also reported to inhibit the development of experimental atherosclerosis (Bordia and Bansel, 1973; Jain et al., 1973). Sainami et al. (1979) have shown that even those consuming small amounts of

garlic and onion are better protected and that a routine consumption of onion and garlic has a protective effect in maintaining low serum lipids at normal/low limits.

Magnesium status in the elderly

Magnesium inadequacy is not uncommon. Epidemiological evidence that soft water and diets with high Ca/Mg ratio increase vulnerability to cardiovascular disease (Anderson et al., 1975) indicates that when magnesium intake too provided by drinking water is low can be critical. Alternative epidemiological studies have suggested that people living in areas with hard water have a higher myocardial magnesium concentration which resulted in a lowered incidence of sudden death due to ischemic heart disease (Anderson et al., 1975). Nevertheless determination of magnesium status is not a routine even in hospital patients with disorders the nature and/or treatment of which cause magnesium loss (Seelig, 1981).

The importance of magnesium in the mineral metabolism of the body is currently receiving increased attention. The body contains approximately 2g of magnesium of which 65% is in muscle and bone.

Magnesium plays many vital roles in the body. It is

an important component of bone. As a coenzyme it has a pivotal position in normal physiology participating in many enzyme systems governing both carbohydrate and protein metabolism. It is concerned with normal neuromuscular functions in both cardiac and skeletal muscle. Cardiac rhythm disturbances have been documented in patients with hypomagnesemia (Enschberg et al., 1950; Chaldla et al., 1972; Iseri et al., 1975) and treatment with magnesium has been described for these abnormalities.

Magnesium deficiency has been thoroughly studied in rats. Briefly this condition results in peripheral vasodilatation, convulsions, a rise in plasma calcium and Nephrocalcinosis, defective coupling of phosphorelation with oxydation and consequently elevated levels of basal metabolism similar conditions have been reported occasionally in man. Convulsions which may be fatal have also been reported (Hanna, 1961).

Fischer and Girowx (1984) found an accumulation of sodium in the myocardium during magnesium deficiency. However the same authors in another article indicated, that though the magnesium deficiency does not exert any effect on the number of sodium potassium pumpsites it does decrease the activity of the pump suggesting that it leads to an

increase in intracellular sodium. This in turn is suggested to change the membrane potential and contribute to arrhythmias associated with magnesium deficiency (Fischer and Girowx, 1986).

Althra and Altura (1981) reviewed the mechanisms underlying the relationship between magnesium and blood pressure. It is indicated that hypomagnesemia potentiates contractibility and attenuates relaxation of vascular smooth muscle in response to neurohormonal substances such as prostaglandins and β -adrenergic amines. It has been postulated that if the concentration of extra cellular magnesium is lowered calcium influx is enhanced and results in an increased contractibility of smooth muscle.

Altura et al (1984) found increased blood pressure with decreasing magnesium levels in the diet. Also Berthelot and Esposito (1983) noted a rapid increase in the blood pressure level and heart rate in rats fed on magnesium deficient diet (0.008%) compared to those fed a normal amount of magnesium (0.2%). Dietary magnesium modifications seem to alter the electrolytes composition in blood and extra cellular fluids resulting in a change in the blood pressure.

A number of workers showed a correlation between vascular disease and the hardness of water (Anderson et al., 1969; Crawford et al., 1971; Editorial: Br. Med. J. 1963) and

magnesium has been suggested as the main protective factor. (Browne 1963; Selig and Heggtvit 1974). Bershon and Oelofse (1957) demonstrated high serum magnesium levels in Bantus than in Europeans. Similarly Charnock et al (1959) found low incidence of myocardial infarction in Europeans and Aborigines in Alice Spring with high serum magnesium levels. On the otherhand Abraham et al (1978) found no association serum magnesium levels and clinically evidenced pressure and absence of Ischemic heart disease. A controversy still thus exists on the physiological role of magnesium and heart diseases.

In hyperthyroidism hypomagnesimia is reported with neuromuscular irritability in patients and a reversal of clinical signs and symptoms after magnesium sulphate therapy (Brown et al., 1958; Lee 1960; Wallach et al., 1962; Harsh and Siddique 1973). This however has been attributed to vasodilator effect of magnesium sulphate.

Harsh and Siddique (1973) studied the role of magnesium in pancreatic enzymes, essential in the digestion of food. Derangement in magnesium may affect pancreatic function. Magnesium levels are often altered in diseases of pancreas. Magnesium deficiency has been reported as a complication of the diseases of small intestine, celiac disease, enteritis childhood malnutrition, chronic renal disease and disorders

of parathyroid (Wallach et al., 1962; Booth et al., 1963). Hypermagnesemia is reported in advanced renal disease and hypothyroidism (Wallach ^{et al}, 1962).

The range of normal serum magnesium levels are not found to show age specific or sex differences and may not necessarily reflect dietary intakes or total body magnesium (Wallach et al., 1962; Kedarnath et al., 1969; Abraham et al., 1978). However, normal levels do not rule out deficiency under very low levels of intake.

Patients with serum magnesium levels less than 1 mEq/lit (1.2 mg/dl) were also found to have hypocalcemia and magnesium supplements are needed where magnesium levels were below 1 mg Eq/lit. (Booth et al., 1973).

Aging is thus associated with several physiological and biochemical changes including those in blood pressure, physical capacity, neuromotor speed, sensory activity, bone loss, body composition and constituents of blood and serum such as blood glucose and serum lipids. Magnesium is also a likely candidate for these changes. Many of these changes are not inevitable concomitants of the aging process and the nature and magnitude of these changes vary with dietary patterns, life styles, non-dietary factors such as cigarette smoking, environmental factors etc.

The present studies were ^{thus} aimed to investigate the role of dietary factors in influencing the crucial facets of life - The fetal growth in relation to maternal status on one hand and the age related changes after cessation of growth on the other.

The area of choice for these studies was Kerala as indicated earlier a state where the diets of the poor present unique features in that not much of fat is consumed by the poor except for small quantities of coconut oil and coconut which are deficient in essential fatty acids (EFA) and tocoferols. As rice and tapioca are the staples consumed and the water is soft the diets of the poor tend to be marginally deficient in magnesium as well.

On the other hand the diets of the upper class consist much more fat, milk, meat and fish and are likely to be more than adequate. In fact the excess consumption of coconut and coconut oil which are highly saturated is likely to be associated with hypercholesterolemia and obesity specially with advancing age.

1. The fetal growth studies were carried out in the low (LIG) and high (HIG) income groups particularly with an interest to see the status of these poorly nourished pregnant and parturient women with regard to changes in body

weight and changes in blood hemoglobin, serum lipids, vitamin E and magnesium.

2. Similarly the aging studies were made to see the age-specific changes starting from 20 years onwards upto 70 years with regard to selected parameters such as somatic measurements, blood glucose serum lipids and magnesium in relation to plane of nutrition and sex differences. The results of these investigations are presented in this thesis.