A REVIEW ON SUPPLEMENTATION OF MICRONUTRIENTS AND ITS EFFECT ON PREGNANCY OUTCOME

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ABSTRACT:

Background: Pregnancy is one of the most important periods in life when increased micronutrients needed by the body; both for the health and well-being of the mother and for the growing fetus and newborn child. A global prevalence of some two billion people at risk of micronutrient deficiencies, and multiple micronutrient deficiencies of many pregnant women in low-middle income group underline the urgency to establishing the optimal recommendations, including for delivery. It has long been recognized that adequate iron is important for best reproductive outcomes, including gestational cognitive development. Similarly, iodine and calcium have been recognized for their roles in development of the fetus/neonate. Less clear effects of deficiencies of zinc, copper, magnesium and selenium have been reported. Folate sufficiency periconceptionally is recognized both by the practice of providing folic acid in antenatal iron/folic acid supplementation and by increasing numbers of countries fortifying flours with folic acid. Other vitamins likely to be important include vitamins B12, D and A with the water-soluble vitamins generally less likely to be a problem. Many antenatal programmes are not currently achieving this.

Aim: The main aim of this review is to address the need for micronutrients during pregnancy, the importance of micronutrient deficiencies during gestation and before and the beneficial effect of antenatal micronutrients supplementation.

Result: The supplementation of iron, folic acid, calcium and vitamin D helped in prevention of preterm delivery, low birth weight infants, Intra uterine growth retardation, small for gestational age and many other metabolic disorders in newborn. Also helped in well-being of pregnant mothers by preventing them from getting into any pregnancy related complication.

Conclusion: It was concluded that antenatal multi-micronutrient supplementation (Folic acid, Iron, Calcium and Vitamin D) had a significant positive effect on pregnancy and its outcome.

Keywords: Antenatal care, micronutrients, pregnant women, pregnancy, recommendation, supplementation.

INTRODUCTION

Every year more than 20 million infants are born with low birth weight worldwide. About 3.6 million infants die during the neonatal period. More than one third of child deaths are thought to be attributable to maternal and child under nutrition [1]. Insufficient supplies of essential vitamins and micronutrients can lead to a state of biological competition between mother and conceptus, which can be detrimental to the health status of both [2]. Micronutrients are necessary for normal growth and development of the fetus and deficiencies have been found to be associated with intrauterine growth retardation and small for gestational age (SGA) infants [3]. Micronutrients deficiencies result from inadequate intake of meat, fruits and vegetables and infections can also be a cause. Multiple micronutrient supplementations in pregnant women may be a promising strategy for reducing adverse pregnancy outcomes. The World Health Organization (WHO) currently recommends iron and folic acid supplementation to reduce the risk of iron deficiency anemia among pregnant women. Several systematic reviews of trials examining the effects of maternal multiple micronutrient supplementation have been conducted but they have had limitations [1]. Out of all the micronutrients this paper focuses on only those which are essential for fetal growth and development and deficiency of which may lead to complication in pregnancy outcome.

ROLE OF IRON IN PREGNANCY

Maternal iron status has been a critical factor for pregnancy outcomes, because maternal anemia as well as iron deficiency increases the risk of adverse pregnancy outcomes such as preterm delivery and low birth weight [4]. Iron is an essential micronutrient that plays an important role in critical cellular functions in all organ systems. It is vital for early brain growth and function because it supports neuronal and glial energy metabolism, neurotransmitter synthesis, and myelination. Low iron stores at birth and IDA (Iron Deficiency Anemia) in infancy may also adversely influence cognitive, emotional, motor, and neurophysiological development in humans, with short- and long-term consequences that are not corrected by iron therapy. [5].

IRON REQUIREMENT

Based on the available data for Indian and Western women, an additional 760 mg required during the entire pregnancy period (includes requirement for fetus + expansion of maternal red cell mass + placenta and cord + obligatory loss) [6].

Iron requirement during pregnancy (Trimester wise):

Trimester	**Requirement (mg)**	
	10 kg GWG	**12 kg GWG**
1st Trimester	130	138
2nd Trimester	320	372
3rd Trimester	310	351
Total	**760**	**861**

Table 1. Research studies on iron intake/supplementation and its effect on pregnancy and its outcome

AUTHOR, YEAR OF PUBLICATION & OBJECTIVE	STUDY DESIGN	METHODOLOGY	RESULTS	CONCLUSION
Ji-Yun Hwang. Et al, 2013 [4] Objective: To find out the association between total iron intake at mid-pregnancy and fetal growth.	A total of 337 women (51 from Seoul, 123 from Cheonan, and 163 from Ulsan) were included in this study.	Iron intake from diet and supplements was examined by a 24-hour recall method. Subjects were divided into three groups based on tertiles of total iron intake levels. Fetal biometry was assessed by ultrasonography at mid-pregnancy.	About 99% of the non-supplement users had iron intake below the RNI for pregnant women (24 mg), whereas 64.9% of supplement users had above the UL (45 mg). In the babies of mothers in the third tertile of iron intake (>17.04 mg), biparietal diameter, AC, and femur length were ↓ by 0.41 cm (P =0.019), 0.41 cm (P = 0.027), and 0.07 cm (P = 0.051), respectively, than the babies of mothers in the second tertile of iron intake (11.49 ~ 17.04 mg).	The results suggest that excessive maternal iron intake at mid-pregnancy is associated with reduced fetal growth. Iron supplementation for pregnant women should be individualized according to their iron status.
Jie Shao. Et al, 2012 [5] Objective: To find out whether maternal serum ferritin concentration is associated with new born iron stores in women with low ferritin status in late pregnancy	Pregnant women aged 20-25 years were recruited. Enrollment criteria included singleton birth, parity ≤ 1 and no maternal chronic disease. Out of total 3891 pregnant women fulfilled the enrollment criteria, 3702 agreed to blood sampling.	Blood sampling and haematologic assessment was done. Blood samples were obtained for 3702 pairs of mothers & their full term singleton neonates. A total of 3603 samples (5ml) were available for maternal Hb & 3684 for SF. Cord blood SF (5ml) was obtained for 3699 neonates & Hb was missing for 456 samples.	Pearson correlations showed low-order relations between maternal & cord blood Hb & maternal & cord blood SF (r values = 0.10 & 0.07, respectively), which were significant due to large n (P ≤ 0.0001). Maternal SF was related to cord-blood SF below the threshold of maternal SF = 13.6 mg/L (b = 2.4; P = 0.001) but not above.	There were no detectable thresholds in the relations between maternal SF and cord-blood Hb or between maternal Hb and either cord-blood iron measure.
Annika helin. Et al, 2012 [13] Objective: To investigate the possible total daily iron intake during	A prospective cohort study (based on cluster-RCT). 399 pregnant women who were at ↑risk of GDM participated in a GDM prevention trial and	GDM was diagnosed with oral glucose tolerance test at 26–28 weeks' gestation or based on a diagnosis recorded in the Finnish Medical Birth registry. Data on iron	GDM was diagnosed in 72 women (18.1%). The OR for total iron intake as a continuous variable was 1.006 (p=0.038). Women in the highest fifth of total daily iron intake had an adjusted OR of 1.66 (p=0.15) for GDM. After	High iron intake during pregnancy ↑ the risk of GDM especially in women who are not anemic

pregnancy, Hb in early pregnancy & risk of GDM in women at ↑ risk of GDM.	were followed throughout pregnancy.	intake was collected using a 181-item FFQ & separate questions for supplement use at 26–28 weeks gestation.	excluding participants with low Hb levels (≤120 g/l) already in early pregnancy the adjusted OR was 2.35 (p=0.023).	in early pregnancy and who are at ↑ risk of GDM.
Ketil Stordal. Et al, 2014 [14] Objective: To determine whether the use of iron supplements during pregnancy affects the risk for celiac disease in children.	The prospective Norwegian Mother and Child cohort study. Complete data were available for 78,846 children (mean age 5.9years, range 2–12 years)	The individuals with celiac disease were identified by answers on questionnaires and linkage to the Norwegian Patient Register.; 314 children were identified with celiac disease. Questionnaires were given to pregnant women to collect information on use of iron-containing supplements, diet, anemia, and levels of hemoglobin.	Celiac disease was diagnosed in 4.65 of 1000 children whose mothers took iron supplements while they were pregnant, compared with 3.15 of 1000 children whose mothers did not. However, celiac disease was not associated with the mother's intake of iron from foods. Anemia before or during the early stages of pregnancy was not significantly associated with the risk of celiac disease in children. The use of iron supplements during pregnancy remained significantly associated with celiac disease in children.	It was found that there was an increased risk of celiac disease in children whose mothers used iron supplements during pregnancy; this association does not appear to arise from maternal anemia.
Suying Chang. Et al, 2013 [15] Objective: To determine the impact of iron deficiency anemia (IDA) in pregnancy on young child development.	A 2-year follow-up of 850 children born to women who participated in a double-blind cluster-RCT of prenatal micronutrient supplementation in western rural China.	These women were randomly assigned to receive either daily folic acid, iron/folic acid (60 mg iron), or multiple micronutrients (with 30 mg iron) during pregnancy. Children were categorized into the prenatal-IDA and prenatal–non-IDA groups based on the mother's Hb in the third trimester. Bayley scales of infant development were administered to the children to assess their development at 3, 6, 12, 18, and 24 months of age.	Compared with the prenatal–non-IDA group, the prenatal-IDA group showed a significantly lower mental development index at 12, 18, and 24 months of age. The adjusted mean difference was 5.8 (95% [CI], 1.1–10.5), 5.1 (95% CI, 1.2–9.0), and 5.3 (95% CI, 0.9–9.7), respectively. Further analysis showed that the mental development indexes in the prenatal-IDA group and prenatal–non-IDA group were similar with supplementation of iron/folic acid but were significantly lower in the prenatal-IDA group with supplementation of folic acid or multiple micronutrients.	Prenatal IDA in the third trimester is associated with mental development of the child. However, prenatal supplementation with sufficient iron protects child development even when the woman's IDA was not properly corrected in pregnancy.
Rebecca J. Schmidt. Et al,	A population-based case-	Mean maternal daily iron intake was	Mothers of cases were less likely to report	Low iron intake

2014 [16] Objective: To examine maternal iron intake and risk of ASD	control study (the Childhood Autism Risks from Genetics and the Environment (CHARGE) Study) from 2003 to 2009 with a diagnosis of ASD (n = 520) or typical development (n = 346) that was clinically confirmed using standardized assessments.	quantified on the basis of frequency, dose, and brands of supplements and cereals consumed each month from 3 months before pregnancy through the end of pregnancy and during breastfeeding (the index period), as reported in parental interviews.	taking iron-specific supplements during the index period (adjusted odds ratio = 0.63, 95% confidence interval: 0.44, 0.91), and they had a lower mean daily iron intake (51.7 (standard deviation, 34.0) mg/day) than mothers of controls (57.1 (standard deviation, 36.6) mg/day; P = 0.03). The highest quintile of iron intake during the index period was associated with reduced ASD risk compared with the lowest (adjusted odds ratio = 0.49, 95% confidence interval: 0.29, 0.82), especially during breastfeeding.	significantly interacted with advanced maternal age and metabolic conditions.↑ maternal iron intake was associated with reduced risk of ASD.

ABBREVIATIONS:

RNI- Recommended Nutrient Intake, UL- Upper Level, AC- Abdominal Circumference, Hb- Hemoglobin, SF- Serum Ferritin, GDM- Gestational Diabetes Mellitus, RCT- Randomised Controlled Trial, OR- Odds Ratio, IDA- Iron Deficiency Anemia, CI- Confidence Interval, ASD- Autism Spectrum Disorder.

INTERPRETATION:

The above mentioned studies highlight the effect of iron intake on pregnancy outcome. Out of the six research studies, three studies stated that increased maternal iron intake (upto 109.9 mg/day) during pregnancy is associated with reduced fetal growth, increased risk of developing gestational diabetes mellitus in those who are not anemic in early pregnancy and increased risk of celiac disease in children after

birth, whereas one study stated that increased intake (upto 80 mg/day) reduced the risk of developing autism spectrum disorder (ASD) in children.

There was one study which stated that there were no detectable thresholds in the relations between maternal serum ferritin and cord blood Hb rather no association between maternal serum ferritin concentration and new born iron stores in women with low ferritin status in late pregnancy.

ROLE OF FOLIC ACID IN PREGNANCY

Women are advised to increase their intake of folic acid 4weeks before conception until 8 weeks after by taking a supplement [7].The role of folic acid deficiency in other birth outcomes, such as low birth weight, pre-term delivery, and peri-natal mortality, is unclear [8].

The important role that folate plays with the progression of pregnancy was recognized in historical reports of the discovery of human folate deficiency that first linked food sources of the vitamin with the treatment of anemia of pregnancy. Both red blood cell and serum folate concentrations are known to decrease significantly throughout an unsupplemented pregnancy. The decline in maternal folate status during pregnancy is generally explained by an increase in requirements for folate associated with the growth of fetal, placenta, and maternal tissue. Folate is required for DNA synthesis and methylation processes, including the remethylation of homocysteine to methionine, and is the major determinant of plasma homocysteine concentrations. Hyperhomocysteinemia has been associated with increased risk of a number of pregnancy complications including NTDs (Neural Tube Defects) [9].

FOLIC ACID REQUIREMENT

Normal folate requirement of women is 200µg/d. An additional requirement of 300 and 100 µg respectively during pregnancy and lactation was decided to be added for meeting the factorial extra needs [6].

Table 2. Research studies on folic acid intake/supplementation and its effect on pregnancy and its outcome

AUTHOR, YEAR OF PUBLICATION & OBJECTIVE	STUDY DESIGN	METHODOLOGY	RESULTS	CONCLUSION
Priscilla A. Zetstra-van der Woude. Et al, 2014 [6] Objective: To investigate the effect of dispensed high-dose folic acid during pregnancy and asthma medication in the offspring.	Data from the pregnancy database IADB.nl, which contains pharmacy-dispensing data of mothers and children from community pharmacies in the Netherlands from 1994 until 2011.	The dispension of asthma medication in children exposed in utero to high-dose folic acid was compared with children who were not exposed to this high dose. Incidence rate ratios (IRRs) with 95% confidence intervals (CIs) were calculated.	In 2.9% (N= 913) of the 39 602 pregnancies in the database, the mother was dispensed high-dose folic acid. Maternal high-dose folic acid was associated with an increased rate of asthma medication among children: recurrent asthma medication IRR = 1.14 (95%CI: 1.04–1.30) and recurrent inhaled corticosteroids IRR = 1.26 (95%CI: 1.07–1.47).	Almost 3% of the children were prenatally exposed to high-dose folic acid. This study suggests that supplementation of high-dose folic acid during pregnancy might ↑ the risk of childhood asthma.
Breige McNulty. Et al, 2013 [8] Objective: To investigate maternal folate and homocysteine responses and related effects in the newborn that resulted from continued FA supplementation after the first trimester of pregnancy.	A double-blinded, RCT. Women in the 1st trimester of pregnancy who were attending antenatal clinics were invited to participate in the Folic Acid Supplementation in the 2nd and 3rd Trimesters (FASSTT) trial. Participants were healthy women with singleton pregnancies, without pregnancy complications, aged between 18 & 35 yrs.	The sample size was estimated by using mean (6SD) red blood cell folate and homocysteine concentrations in women who had taken (or not taken) FA supplements from our previous observational study. We estimated that a sample size of 60 subjects per group would be able to discriminate a difference in homocysteine concentration of 0.5 mmol/L between placebo and treatment groups with a power of 80% at a = 0.05	A total of 119 women (60 women in the placebo group; 59 women in the treatment group) completed the trial. From GWs 14– 36, mean (6SD) serum folate decreased (P, 0.001) in unsupplemented women, whereas plasma homocysteine increased (6.6 6 2.3 to 7.6 6 2.3 mmol/L; P, 0.001). However, FA supplementation prevented these changes & resulted in a significant ↑ in red blood cell folate concentrations from 1203 6 639 to 1746 6 683 nmol/L (P , 0.001; GWs 14–36). Cord blood folate was significantly higher in the FA group than in the placebo group (P = 0.001)	The study supports that continued supplementation with 400 mcg FA/d in trimesters 2 and 3 of pregnancy can ↑ maternal and cord blood folate status and prevent the ↑ in homocysteine concentration that otherwise occurs in late.
K. Pentieva. Et al, 2012	Mother–child pairs (n = 39)	Anthropometric measurements	Children of mothers who received FA	This pilot study suggests that

[17] Objective: To investigate the effect of folic acid supplementation during pregnancy on growth and cognitive development of young children	were recruited from a previously conducted RCT which investigated the effect of FA supplementation (400 mg/day) in the second and third trimester of pregnancy (FASSTT) study.	including height, weight, and waist circumference were taken in order to assess the physical development of the children at the age of 2.8 years. At the same time, (BSITD), III edition was employed to evaluate the following five domains of child development: cognitive, receptive communication, expressive communication, fine and gross motor skills.	supplementation during the 2nd & 3rd trimester of pregnancy compared to those that did not showed significantly higher scores in the cognitive domain of infant development assessment after adjustment for maternal age, socio-economic factors and birth weight. The differences between the two groups in the other developmental domains of BSITD were not found to be significant. No significant differences in anthropometric measurements were observed between children born to mothers in the placebo and FA treatment groups.	FA supplement use during later pregnancy may confer an enhanced effect on the cognitive ability of young children.
Jonathan P. Bestwick. . Et al, 2014 [18] Objective: To study the relation between FA supplementation and prevention of NTD.	Assess the extent of folic acid supplementation using data from almost half a million women screened at the Wolfson Institute between 1999 and 2012. 466,860 women screened provided details on folic acid supplementation	The proportion of women who took folic acid supplements before pregnancy was determined according to year and characteristics of the women. All the data were anonymous and no enquiries or procedures were performed other than those that formed part of the routine service so ethical approval was not required.	The proportion of women taking FA supplements before pregnancy declined from 35% in 1999–2001 to 31% in 2011–2012. 6% of women age under 20 took FA supplements before pregnancy compared with 40% of women aged between 35 and 39. Non-Caucasian women were less likely to take FA supplements before pregnancy than Caucasian women; Afro-Caribbean 17%, Oriental 25% and South Asian 20% compared with 35% for Caucasian women.	The results show that public health policy cannot rely on pre-pregnancy FA supplementation alone. About 80% of all the NTD's could be prevented if FA supplementation were 5mg instead 0.4mg (RDD of FA).
Mie Shiraishi. Et al, 2012 [19] Objective: To evaluated the validity & reproducibility of intakes of folate and vitamin B12 estimated	A sample of 167 healthy subjects with singleton pregnancies in the second trimester was recruited at a private obstetric hospital in metropolitan Tokyo from June to October 2008 (n =	The dietary intakes of folate and vitamin B12 were assessed using the DHQ. The serum concentrations of folate and vitamin B12 were measured as reference values in the validation study. To assess the reproducibility of the results, 58	Significantly positive correlations were found between energy-adjusted intakes and serum concentrations of folate and vitamin B12 ($r = 0.286$, $p < 0.001$ and $r = 0.222$, $p = 0.004$, respectively). After excluding the participants with nausea (n = 121), the correlation coefficient for	The present study indicated that the DHQ had acceptable validity and reproducibility for assessing folate and vitamin B12 intakes in Japanese pregnant women.

from a self-administered DHQ in Japanese pregnant women.	76), & at a university hospital in Tokyo from June 2010 to June 2011 (n = 91).	pregnant women completed the DHQ twice within 4-5 week interval.	vitamin B12 increased to 0.313 (p = 0.001). The intra class correlation coefficients of the two-time DHQ were 0.725 for folate and 0.512 for vitamin B12.	
Dervla Kelly. Et al, 2012 [20] Objective: To identify factors associated with suboptimal peri-conceptional use of folic acid and its potential effect on oral clefts.	A cross-sectional analysis of the first wave of data from the infant cohort of the Growing Up in Ireland study. A systematic selection procedure, based on a random start and constant sampling fraction, was used. The 11134 infants representing the 9-month cohort were born between 1 December 2007 and the 30 June 2008.	Data collection comprised questionnaires conducted by interviewers with parents in parents' homes. Characteristics of mothers who did or did not take folic acid before and during pregnancy, as well as the effect of folic acid use on the prevalence of cleft lip and palate were recorded.	The prevalence of cleft lip and palate was 1.98 (95%confidence interval [CI] = 1.31 to 2.99) per 1000 9-month-olds. The odds ratio for cleft lip was 4.36-fold higher (95%CI = 1.55 to 12.30,P = 0.005) for infants of mothers who did not take folic acid during the first 3months of pregnancy, when compared with those who did have a folate intake during the first trimester. Folic acid use was suboptimal in 36.3% (95%CI = 35.4 to 37.2) of the sample.	The findings support the hypothesis that taking FA may partially prevent cleft lip and palate. They are particularly relevant for GPs, because they are usually the first port of call for women before and during early pregnancy.

ABBREVIATIONS:

IRR- Incidence Rate Ratio, GW- Gestational weight, FA- Folic Acid, RCT- Randomised Controlled Trial, BSITD- Bayley Scales of Infant and Toddler Development, NTD- Neural Tube Defect, DHQ- Diet History Questionnaire, RDD- Recommended Daily Dose, GP- General Practice.

INTERPRETATION:

The above mentioned studies highlight the role of folic acid in pregnancy outcome. Out of the six research studies two studies stated that high dose of folic acid (400 mcg/day in trimesters 2 and 3 of pregnancy) can increase maternal and cord blood folate status and prevent the increase in homocysteine concentration that otherwise occurs in late also may confer an enhanced effect on the cognitive ability of young children whereas one study stated that supplementation of high-dose folic acid (>0.5mg/day) during pregnancy might increase the risk of childhood asthma.

There was one study which claimed that about 80% of all the NTD's could be prevented if folic acid supplementation were 5mg instead 0.4mg which was recommended daily dose of folic acid. Another study which supported the hypothesis that taking folic acid may partially prevent cleft lip and palate.

ROLE OF CALCIUM IN PREGNANCY

There are biological limits to a pregnant woman's capacity to increase calcium absorption, and if she does not consume adequate amounts of dietary calcium, she may be at increased risk for gestational complications, such as preeclampsia, and preterm delivery or long-term morbidities, such as excessive bone loss.

Women who begin pregnancy with adequate intake may not need additional calcium, but women with suboptimal intakes (<500 mg) may need additional amounts to meet both maternal and fetal bone requirements. Women who chronically consume low amounts of calcium (<500 mg/day) may be at risk for increased bone turnover during pregnancy. High calcium intake is associated with improved calcium balance, perhaps providing a protective effect against bone loss during pregnancy [10].

CALCIUM REQUIREMENT

The balance data from adults have indicated that intakes in the range of 500-600 mg/d are necessary for positive calcium balance. Using factorial method, calcium intake needed to maintain calcium adequacy was obtained for pregnant and lactating women which were double the normal requirement that is 1200 mg/d [6].

Table 3. Research studies on calcium intake/supplementation and its effect on pregnancy and its outcome

AUTHOR, YEAR OF PUBLICATION & OBJECTIVE	STUDY DESIGN	METHODOLOGY	RESULTS	CONCLUSION
Landing MA Jarjou. Et al, 2013 [21] Objective: To investigate whether Calcium supplementation of pregnant gambian women with a low calcium intake results in lower maternal bone mineral content in the subsequent lactation.	All women in the calcium supplementation trial who had been scanned with dual-energy X-ray absorptiometry at 52 wk of lactation (L52; n = 79) were invited for follow-up when for ≥3 mo (NPNL) or at 52 wk postpartum in a future lactation (F52).	Women were randomly assigned, double-blind and in a permuted block of 4, to receive a supplement that contained 1500 mg Ca/d (3 calcium carbonate tablets; Calcichew; Nycomed Pharma AS; distributed by Shire Pharmaceuticals) or matched placebo (microcrystalline cellulose and lactose; Nycomed Pharma AS) from 20 wk of pregnancy to delivery.	Sixty-eight women participated (35 at both NPNL and F52 and 33 at only one time point). The mean (±SD) time from L52 was 4.9 ± 1.9 y for NPNL and 5.0 ± 1.3 y for F52. SA-BMC was > at NPNL than at L52 in the placebo group (P ≤ 0.001) but not in the calcium group (P for time-by-group interaction: lumbar spine, 0.002; total hip, 0.03; whole body, 0.03). No significant changes in SA-BMC from L52 to F52 were observed in either group. Consequently, the < SA-BMC in the calcium group at L52 persisted at NPNL and F52 (P ≤ 0.001)	In rural Gambian women with a low-calcium diet, a calcium supplement of 1500 mg/d during pregnancy resulted in ↓ maternal bone mineral content in the subsequent lactation that persisted long term.
Keiko Tanaka. Et al, 2012 [22] Objective: To investigate the association between maternal intake of dairy products and calcium during pregnancy and the risk of childhood dental caries.	It was a prospective cohort study. Of the 3,639 eligible pregnant women in Neyagawa City, 627 participated in the OMCHS between November 2001 & March 2003. Later, 375 pregnant women living in municipalities were also recruited. Ultimately, a total of 1,002 pregnant women	Data on maternal intake during pregnancy were assessed through a diet history questionnaire. Outcome data was collected at 41–50 months of age. Children were classified as having dental caries if one or more primary teeth had decayed or been filled.	↑ maternal cheese intake during pregnancy was significantly inversely associated with the risk of dental caries in children, showing a clear inverse dose–response relationship; the adjusted OR in comparison of the highest tertile with the lowest was 0.37 (95 % CI: 0.17-0.76, P for trend = 0.01). The inverse associations between maternal intake of total dairy products, yogurt, and calcium during pregnancy and the risk of childhood	The study concluded that high intake of maternal cheese during pregnancy may reduce the risk of childhood dental caries.

	between the 5th & 39th week of pregnancy gave their fully informed consent &completed the baseline survey.		dental caries were of borderline significance. There was no evident relationship between maternal milk intake and the risk of childhood dental caries.	
Adrienne S Ettinger. Et al, 2014 [23] Objective: To evaluate the effect of dietary calcium supplementation on bone turnover during pregnancy and the early postpartum period.	In a double-blind, randomized placebo-controlled trial, we randomly assigned 670 women in their first trimester of pregnancy to 1,200 mg/day calcium (N = 334) or placebo (N = 336).	Subjects were followed through 1-month postpartum and the effect on urinary cross-linked NTx of type I collagen, a specific marker of bone resorption, was evaluated using an intent-to-treat analysis. Women with a baseline & at least one follow-up measurement (N = 563; 84%) were included. Subsequent analyses were conducted stratifying subjects by compliance assessed using pill counts. In random subsets of participants, bone-specific alkaline phosphatase (BAP) (N = 100) and quantitative ultrasound (QUS) (N = 290) were also measured.	Calcium was associated with an overall reduction of 15.8% in urinary NTx relative to placebo ($p < 0.001$). Among those who consumed ≥50%, ≥67%, and ≥75% of pills, respectively, the effect was associated with 17.3%, 21.3%, and 22.1% reductions in bone resorption (all $p < 0.001$). There was no significant effect of calcium on bone formation measured by BAP. However, by 1-month postpartum, those in the calcium group had significantly lower NTx/BAP ratios than those in the placebo group ($p = 0.04$) indicating a net reduction in bone loss in the supplement group by the end of follow-up.	Calcium administered during pregnancy and the early postpartum period, to women with intakes around adequacy, was associated with reduced bone resorption and, thus, may constitute a practical intervention to prevent transient skeletal loss associated with childbearing.
Ulrike Trautvetter. Et al, 2014 [24] Objective: To determine the effect of calcium phosphate and/or vitamin D3 on bone and mineral metabolism.	Sixty omnivorous healthy subjects (men, n = 24; women, n = 36) participated in this double-blind, placebo-controlled parallel designed study. Eligibility criteria for participants were age between 20 and 70 years and physical health. Four	All subjects documented their normal nutritional habits in a dietary record for 3 successive days. After baseline, subjects were allocated to three intervention groups: CaP (additional 1 g calcium/d), vitamin D3(additional 10 µg/d) and CaP + vitamin D3. In the last week of each study period (baseline, placebo, after 4 and 8 weeks of intervention), a faecal (three days)	After four and eight weeks, CaP and CaP + vitamin D3 supplementations increased faecal excretion of calcium and phosphorus significantly compared to placebo. Due to the vitamin D3 supplementations (vitamin D3, CaP + vitamin D3), the plasma 25-(OH)D concentration significantly increased after eight weeks compared to placebo. The additional application of CaP led to a	Supplementation with daily 10 µg vitamin D3 significantly ↑ plasma 25-(OH)D conc. The combination with daily 1 g Ca (as CaP) has a further increasing effect on the 25-(OH)D conc. Both CaP alone and in combination with vitamin D3 have no beneficial effect on bone remodelling

	participants dropped out because of pregnancy, illness and personal reasons.	and a urine (24 h) collection and a fasting blood sampling took place. Calcium, phosphorus, magnesium and iron were determined in faeces, urine and blood. Bone formation and resorption markers were analysed in blood and urine.	significant increase of the 25-(OH)D concentration already after four weeks. Bone resorption and bone formation markers were not influenced by any intervention.	markers and on mineral metabolism.
Deepa V Kanagal. Et al, 2014 [25] Objective: The aim of this study was to find out the relationship of serum levels of calcium and magnesium in pre-eclamptic pregnancies compared to normal pregnancies in women from southern coastal India.	A double blinded case-control study. The study population was pregnant women. 120 women were included in the study, of whom 60 were with pre-eclampsia and the other 60 were normal pregnant women who were taken as controls. All participants were in the 3rd trimester of pregnancy with a GA of >32 weeks, primi or multigravida and with a single fetus.	A detailed family and medical history were taken. Thorough clinical examination was done in all the subjects. Systolic and diastolic blood pressure was carefully recorded. Urine analysis was done in all subjects to measure the degree of proteinuria. Blood was taken from the ante cubital vein using a sterile needle and syringe. Samples were allowed to clot and then centrifuged at 3000 revolutions per minute for 10 minutes. Serum calcium and magnesium level was measured by Colorimetric method.	The serum calcium concentration was significantly lower in the pre-eclamptic group compared to normotensives (7.84 ± 0.87 mg/dl Vs 8.97± 0.69 mg/dl, p<0.001) whereas the levels of serum magnesium showed a marginal difference in both the groups. (1.43± 0.55 mg/dl Vs, 1.57 ± 0.72 mg/dl P 0.257) The study also showed that pre-eclamptic women were older, their BMI was higher and birth weight of babies lower compared to normotensives.	According to the results of the research, intake of supplements, mainly calcium may help in the reduction of incidence of pre-eclampsia especially in a population of a developing country like ours where the nutrition is poor.
Theresa O Scholl. Et al, 2014 [26] Objective: It was hypothesized that stress to maternal calcium metabolism, rather than a low calcium intake or insufficient vitamin D	A prospective cohort study of pregnancy outcome and complications in young, generally healthy women. We studied 1116 participants from the cohort with data on 25(OH)D, total calcium intake (from diet and supplements), and PTH	Socioeconomic, demographic, lifestyle, and dietary data were obtained by in-person interviews at entry to prenatal care (20 wk of gestation) and were updated at weeks 20 and 28. A 24-h recall of the previous day's diet was obtained on the same schedule. Food models were used to estimate portion size with	When 25(OH)D was insufficient, even a high calcium intake was unable to maintain PTH or to moderate the proportion of patients with an elevated PTH. When examined one at a time, very low calcium intake (60% of EAR), very low 25(OH)D (,12 ng/mL), and elevated PTH (.62 pg/mL) each had a small but significant association with birth weight.	It was concluded that maternal calcium metabolic stress, rather than low calcium intake or insufficient vitamin D, has an adverse influence on fetal growth.

status, influences fetal growth.	who enrolled & delivered a live born infant between 2001 and 2007. Informed written consent was obtained from each participant after the purpose of the study was explained.	dietary probes for forgotten foods and unspecified items [eg, if cream or milk (whole, 1%, 2%, skim) was used in coffee or tea]. The type, frequency, and duration of supplement use, was obtained at each visit and from before pregnancy, including whether or not the supplement was prescribed.	Elevated PTH accompanied by insufficient 25(OH)D or very low calcium intake was associated with a 2- to 3-fold increased risk of SGA birth and a significantly LBW, birth length, and HC, even after women who developed preeclampsia were excluded.	

ABBREVIATIONS:

NPNL- Neither Pregnant Nor Lactating, SA-BMC- Size-Adjusted Bone Mineral Content, OMCHS- Osaka Maternal And Child Health Study, OR- Odd Ratio, CI- Confidence Interval, BAP- Bone-Specific Alkaline Phosphatase, NTx- N-Tellopeptides, GA- Gestational Age, LBW- Low Birth Weight, HC- Head Circumference.

INTERPRETATION:

The above mentioned studies highlight the role of calcium in pregnancy outcome. Out of all six research studies four studies showed a positive association of calcium with pregnancy. It has been proved that adequate intake of calcium (1500 mg/d)) during pregnancy resulted in decrease maternal bone mineral content in the subsequent lactation that persisted long term, may reduce the risk of childhood dental carries, reduced bone resorption and, thus, may constitute a practical intervention to prevent transient skeletal loss associated with childbearing and may help in the reduction of incidence of pre-eclampsia especially in a population of a developing country like ours where the nutrition is poor.

One of the study showed both CaP alone and in combination with vitamin D3 have no beneficial effect on bone remodelling markers and on mineral metabolism and in one study it was concluded that maternal calcium metabolic stress, rather than low calcium intake or insufficient vitamin D, has an adverse influence on fetal growth.

ROLE OF VITAMIN D IN PREGNANCY

Vitamin D deficiency has become a common problem globally. It has been estimated that one billion people worldwide are vitamin D deficient. In pregnant women, the prevalence is even greater, especially among women with dark skin color or who have other risk factors. The skeletal benefits of vitamin D are well established, but there is evidence to suggest that vitamin D may also play a role in non-skeletal conditions [11].

The classical function of vitamin D is related to calcium and phosphate homeostasis and bone mineralization. Research over the last 30 years has revealed that vitamin D receptors are present in almost all body tissues, and there is increasing evidence that vitamin D is involved in a variety of processes in the body, including immunity. Furthermore, immune cells, such as macrophages and dendritic cells as well as activated T cells and B cells, express the enzyme 1a-hydroxylase (CYP27B1), which is responsible for converting the major circulating metabolite of vitamin D, 25-hydroxy-vitamin D (25-OH D), to 1a,25-dihydroxyvitamin D [1,25-(OH)2D], the active form of vitamin D. In autoimmune diseases, vitamin D is thought to have a protective effect, probably by enhancing immunologic tolerance. Serum levels of 25-OH D are an accepted measure of the total vitamin D status, regardless of the source of vitamin D [1]

VITAMIN D REQUIREMENT

The WHO Expert Committees recommended 100 Units (2.5 µg) /d for adult males in 1988 and increased them later in 2005 to 200 Units (5 µg)/d. This is obviously due to progressive decrease in the exposure to sunlight and the need to obtain the requirements from dietary and supplement sources. Hence, many foods such as milk and vegetable oils are subjected to mandatory fortification with vitamin D in the developed countries [6].

Table 4. Research studies on vitamin D intake/supplementation and its effect on pregnancy and its outcome

AUTHOR, YEAR OF PUBLICATION & OBJECTIVE	STUDY DESIGN	METHODOLOGY	RESULTS	CONCLUSION
Constance Yap. Et al, 2014 [10] Objective: To investigate the effects of vitamin D supplementation on glucose metabolism during pregnancy.	A double-blind randomized controlled trial of low-dose (LD) versus HD vitamin D3 supplementation. Women with singleton pregnancies who were age 18 years or older and at a gestational age of, 20 weeks at study entry were eligible to participate.	Baseline blood tests, including plasma 25OHD, random BGL, HbA1c, parathyroid hormone (PTH), liver function tests, and serum calcium, were performed at recruitment. A medical history and examination were performed. Participants completed a questionnaire about sunlight exposure and pregnancy multivitamin intake. Ethnicity was self-reported by the participants.	There was no difference in maternal glucose levels on OGTT. Twelve LD women (13%) developed GDM versus seven (8%) HD women (P = 0.25). Neonatal cord 25OHD was higher in HD offspring (46 6 11 vs. 29 6 12 ng/mL, P < 0.001), & deficiency was more common in LD offspring (24 vs. 10%, P = 0.06). Post hoc analysis in LD women showed an inverse relationship between pretreatment 25OHD and both fasting and 2-h blood glucose level on OGTT (both P < 0.001). Baseline 25OHD remained an independent predictor after multiple regression analysis.	HD vitamin D supplementation commencing at a mean of 14 weeks' gestation does not improve glucose levels in pregnancy. However, in women with baseline levels <32 ng/mL, 5,000 IU per day was well tolerated and highly effective at preventing neonatal vitamin D deficiency.
Ingvild M. Sørensen. Et al, 2012 [11] Objective: To estimate whether lower maternal serum 25-OH D concentrations during late pregnancy were associated with an increased risk of childhood-onset type 1-diabetes in the	All pregnant women in 11 of 19 counties in Norway participated. case-control study nested within a cohort of 29,072 women in Norway, 25-OH D levels were measured using a radioimmunoassay on samples from late pregnancy in 109 women delivering a child who developed type 1	One to four blood samples was collected from each woman throughout pregnancy in their respective primary health care centers at regular maternity check-ups. All samples were sent to the Norwegian Institute of Public Health in Oslo. After testing for T. gondii antibodies, in accordance with the original study objective, the sera were stored at 220°C. Subsequent to the	Dividing the levels of maternal 25-OH D into quartiles, there was a trend toward a higher risk of type 1 diabetes with lower levels of vitamin D during pregnancy. The odds of type 1 diabetes was more than twofold higher for the offspring of women with the lowest levels of 25-OH D compared with the offspring of those with levels above the upper quartile.	There was an association between lower maternal serum concentrations of 25-OH D during pregnancy and increased risk of type 1 diabetes development in childhood.

offspring.	diabetes before 15 years of age (case subjects) and from 219 control women.	toxoplasmosis study, all women were asked by mail to participate in additional research, of whom 29,072 women consented.		
Andrew J. O. Whitehouse. Et al, 2012 [27] Objective: To determine the association between maternal serum 25(OH)-vitamin D concentrations during a critical window of fetal Neuro development and behavioral, emotional, and language outcomes of offspring.	A large-scale longitudinal Study. Participants were from the Western Australian Pregnancy Cohort (Raine). Inclusion criteria were a gestational age between 16 and 20 weeks, English language skills sufficient to understand the study demands, an expectation to deliver at King Edward Memorial Hospital, and an intention to remain in Western Australia to enable future follow-up of their child.	Serum 25(OH)-vitamin D concentrations of 743 Caucasian women in Perth, Western Australia (32°S) were measured at 18 weeks pregnancy and grouped into quartiles. Offspring behavior was measured with the Child Behavior Checklist at 2, 5, 8, 10, 14, and 17 years of age (n range = 412–652). Receptive language was assessed with the Peabody Picture Vocabulary Test Revised at ages 5 (n = 534) and 10 (n = 474) years. Raw scores were converted to standardized scores, incorporating cutoffs for clinically significant levels of difficulty.	x2 analyses revealed no significant associations between maternal 25(OH)-vitamin D serum quartiles and offspring behavioral/ emotional problems at any age. In contrast, there were significant linear trends between quartiles of maternal vitamin D levels and language impairment at 5 and 10 years of age. Multivariate regression analyses, incorporating a range of confounding variables, found that the risk of women with vitamin D insufficiency (≤46 nmol/L) during pregnancy having a child with clinically significant language difficulties was increased close to twofold compared with women with vitamin D levels >70 nmol/L.	Maternal vitamin D insufficiency during pregnancy is significantly associated with offspring language impairment. Maternal vitamin D supplementation during pregnancy may reduce the risk of developmental language difficulties among their children.
Eva Morales. Et al, 2012 [28] Objective: To determine whether maternal circulating 25-hydroxyvitamin D (25[OH]D) concentrations in pregnancy are	A population-based mother and child cohort study. 2680 pregnant women were recruited. A total of 2502 women were followed until delivery. Circulating levels of vitamin D in pregnancy were measured in 2258 women. Information on wheezing was	Maternal circulating 25(OH)D concentrations were measured in pregnancy (mean gestational age =12.6 [SD = 2.5] weeks). When the child was age 1 year, parents were asked if their child had a physician-confirmed history of LRTI or a history of wheezing. The questions about wheezing were repeated	The median maternal circulating 25(OH)D concentration in pregnancy was 29.5 ng/mL (interquartile range, 22.5–37.1 ng/mL). After multivariable adjustment, there was a trend for an independent association between higher levels of maternal circulating 25(OH)D levels in pregnancy and decreased odds of lower respiratory tract infections in	Higher maternal circulating 25(OH)D concentrations in pregnancy were independently associated with lower risk of lower respiratory tract infections in offspring in the first year of life but not with wheezing or asthma in childhood.

associated with risk of lower respiratory tract infections, wheezing, and asthma in the offspring.	available for 1724 children, information on LRTI episodes was collected for 1693 children.	annually thereafter. Asthma was defined as parental report of doctor diagnosis of asthma or receiving treatment at the age of 4–6 years or wheezing since the age of 4 years.	offspring. We found no association between 25(OH)D levels in pregnancy and risk of wheezing at age 1 year or 4 years, or asthma at age 4–6 years.	
Lisa M. Bodnar. Et al, 2009 [29] Objective: To examine the association between maternal vitamin D status and the prevalence of BV in early pregnancy.	A prospective cohort study of pregnant women. Eligible women self-reported their race as black or white, had singleton pregnancies, and had no known preexisting conditions, vaginal bleeding, fetal anomalies, or current or planned cervical cerclage. 552 women agreed to participate in the study. Enrollment took place at , <16 wk of gestation [9.5 ± 3.2 wk (mean ±SD)] after women provided informed, written consent.	Women completed an interviewer-administered questionnaire to collect data on socio demographic characteristics; medical, reproductive, and sexual history; and maternal behaviors. Also at enrollment, women provided a non fasting blood sample and underwent a standard pelvic examination. Of the 552 women who enrolled in the study, 526 had complete data available to diagnose BV. From this cohort, we excluded 57 women due to missing first-trimester serum (n = 43) or not completing the baseline interview (n = 14). The final analytical sample was n = 469.	41% of women had BV & 52% had a serum 25(OH)D conc, 37.5 nmol/L. The mean unadjusted serum 25(OH)D conc was lower among BV cases (29.5 nmol/L; 95% CI: 27.1, 32.0) compared with women with normal vaginal flora (40.1 nmol/L; 95% CI: 37.0, 43.5; P , 0.001). BV prevalence decreased as vitamin D status improved (P<0.001). Approximately 57% of the women with a serum 25(OH)D conc, 20 nmol/L had BV compared with 23% of women with a serum 25(OH)D conc.80 nmol/L. There was a dose-response association between 25(OH)D and the prevalence of BV. The prevalence ↓ as 25(OH)D ↑ to 80 nmol/L, then reached a plateau.	The findings suggest that vitamin D deficiency is associated with BV at 16 wk of pregnancy. A better understanding of the vitamin D-BV relation will be ascertained with prospective studies of "incident" BV infections, persistent infections, and infections that spontaneously resolve.
Sedigheh Soheilykhah. Et al, 2013 [30] Objective: To assess the effects of different doses of vitamin D on insulin resistance during pregnancy.	It randomized clinical trial, 120 pregnant women were recruited from two prenatal clinics in Yazd, Iran. Exclusion criteria consisted of women with diabetes or gestational diabetes treated with insulin, women with thyroid or parathyroid disorders, PCOD	The women were divided into three groups randomly. Group A received 200 IU vitamin D daily, group B 50 000 IU vitamin D monthly and group C 50 000 IU vitamin D every 2 weeks from 12 weeks of pregnancy until delivery. The serum levels of fasting blood sugar (FBS), insulin, calcium and 25-hydroxyvitamin D were measured	The mean ±standard deviation of serum 25-hydroxyvitamin D increased in group C from 7.3±5.9 to 34.1±11.5 ng/ml and in group B it increased from 7.3±5.3 to 27.23±10.7 ng/ml, but the level of vitamin D in group A increased from 8.3±7.8 to 17.7±9.3 ng/ml (p<0.001). The mean differences of insulin and HOMA-IR before and after intervention in	The study has shown that supplementation of pregnant women with 50000 IU vitamin D every 2 weeks improved insulin resistance significantly.

	before pregnancy, BMI before pregnancy of >30 kg/m2.	before and after intervention. We used the homeostatic model assessment of insulin resistance (HOMA-IR) as a surrogate measure of insulin resistance.	groups A and C were significant (p=0.01, p=0.02).	

ABBREVIATIONS:

LD- Low dose, HD- High dose, LRTI- Lower Respiratory Tract Infection, BV- Bacterial Vaginosis, PCOD- Polycystic Ovarian Disease, BMI- Body Mass Index.

INTERPRETATION:

The above mentioned research studies highlight the role of vitamin D in pregnancy outcome. Out of six studies one study proved that higher maternal circulating 25(OH)D concentrations in pregnancy were independently associated with lower risk of lower respiratory tract infections in offspring in the first year of life but not with wheezing or asthma in childhood whereas another study of high dose vitamin D supplementation commencing at a mean of 14 weeks gestation does not improve glucose levels in pregnancy. However, in women with baseline levels <32 ng/mL, 5,000 IU per day was well tolerated and highly effective at preventing neonatal vitamin D deficiency.

There was an association between lower maternal serum concentrations of 25-OH D during pregnancy and increased risk of type 1 diabetes development in childhood also there is significant association between insufficient maternal vitamin D levels and offspring language impairment. Maternal vitamin D supplementation during pregnancy may reduce the risk of developmental language difficulties among their children. One of the findings suggested vitamin D deficiency is associated with bacterial vaginosis at 16 wk of pregnancy.

One of the study showed that supplementation of pregnant women with 50000 IU vitamin D every 2 weeks improved insulin resistance significantly.

DISCUSSION:

This review article summarized the effect of multi-micronutrient supplementation during pregnancy. The results indicated that antenatal multi-micronutrient supplementation had a significant positive effect on pregnancy and its outcome. Four micronutrients iron, folic acid, calcium and vitamin D were considered in this review. Each micronutrient and its association with pregnancy were stated in the above tables with the help of few research studies.

It was seen that out of the six research studies, three studies stated that increased maternal iron intake (upto 109.9 mg/day) during pregnancy is associated with reduced fetal growth, increased risk of developing gestational diabetes mellitus in those who are not anemic in early pregnancy and increased risk of celiac disease in children after birth, whereas one study stated that increased intake (upto 80 mg/day) reduced the risk of developing autism spectrum disorder (ASD) in children. There was one study which stated that there were no detectable thresholds in the relations between maternal serum ferritin and cord blood Hb rather no association between maternal serum ferritin concentration and new born iron stores in women with low ferritin status in late pregnancy.

It was seen that out of the six research studies two studies stated that high dose of folic acid (400 mcg/day in trimesters 2 and 3 of pregnancy) can increase maternal and cord blood folate status and prevent the increase in homocysteine concentration that otherwise occurs in late also may confer an enhanced effect on the cognitive ability of young children

whereas one study stated that supplementation of high-dose folic acid (>0.5mg/day) during pregnancy might increase the risk of childhood asthma. There was one study which claimed that about 80% of all the NTD's could be prevented if folic acid supplementation were 5mg instead 0.4mg which was recommended daily dose of folic acid. Another study which supported the hypothesis that taking folic acid may partially prevent cleft lip and palate.

It was seen that out of all six research studies four studies showed a positive association of calcium with pregnancy. It has been proved that adequate intake of calcium (1500 mg/d)) during pregnancy resulted in decrease maternal bone mineral content in the subsequent lactation that persisted long term, may reduce the risk of childhood dental carries, reduced bone resorption and, thus, may constitute a practical intervention to prevent transient skeletal loss associated with childbearing and may help in the reduction of incidence of pre-eclampsia especially in a population of a developing country like ours where the nutrition is poor. One of the study showed both CaP alone and in combination with vitamin D3 have no beneficial effect on bone remodelling markers and on mineral metabolism and in one study it was concluded that maternal calcium metabolic stress, rather than low calcium intake or insufficient vitamin D, has an adverse influence on fetal growth.

Out of six studies one study proved that higher maternal circulating 25(OH)D concentrations in pregnancy were independently associated with lower risk of lower respiratory tract infections in offspring in the first year of life but not with wheezing or asthma in childhood whereas another study of high dose vitamin D supplementation commencing at a mean of 14 weeks gestation does not improve glucose levels in pregnancy. However, in women with baseline levels <32 ng/mL, 5,000 IU per day was well tolerated and highly effective at preventing neonatal vitamin D deficiency. There was an association between lower maternal serum concentrations of 25-OH D during pregnancy and increased risk of type 1 diabetes development in childhood also there is significant association between insufficient maternal vitamin D levels and offspring language impairment. Maternal vitamin D supplementation during pregnancy may reduce the risk of developmental language difficulties among their children. One of the findings suggested vitamin D deficiency is associated with bacterial vaginosis at 16 wk of pregnancy. One of the study showed that supplementation of pregnant women with 50000 IU vitamin D every 2 weeks improved insulin resistance significantly.

CONCLUSION:

This review shows the beneficial effect of antenatal multiple micronutrients supplementation on birth outcomes in pregnancy. It was seen that maternal micronutrients insufficiency significantly co-relates with the adverse outcomes of their offspring and not only this but also has long term intergenerational impact on offspring. Thus micronutrients supplementation was considered to be a potential cost-effective and practical strategy to combat the global nutritional challenge of children and women.

The supplementation of iron, folic acid, calcium and vitamin D helped in prevention of preterm delivery, low birth weight infants, Intra uterine growth retardation, small for gestational age and many other metabolic disorders in newborn. Also helped in well-being of pregnant mothers by preventing them from getting into any pregnancy related complication.

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