

*Full Length Research Paper*

# **Maternal vitamin D deficiency triggering rickets in their breastfeeding infants: a current study and Literature Review**

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Abstract

The aim of this study is to confirm our original hypothesis that maternal deficiency of vitamin D is a major factor in development of rickets in her breastfeeding infant and review the literature. In six months from October 2008 to March 2009 out of 136 infants with diagnosis of clinical rickets, seen in Medinah Maternty and Chlidrens Hospital, 40 infants and their mothers were included in this study. Socioeconomical data were recorded. Blood samples were collected for biochemical and for parathormone and vitamin D (25OHD) levels from both mother and baby. Radiology of wrist was done for each infant. All cases were divided to three age groups. Results from pairs were available. On comparing parathormone (MPTH) in mothers of children (CPTH) with active rickets and healed rickets. MPTH was 94.8 and CPTH 199.9, this was considered significant at P value .0104. As for children with healed rickets and their mother's PTH the mean PTH was 199.8 in active rickets and 60.8 in healed rickets, the P value is 0.002 which is very significant. The 25OHD levels in mother and breastfed infants with active rickets were very low in infants with active rickets and low in their mothers. In the healed group 25OHD was significantly high in infants but not in mothers. The hypothesis that maternal vitamin D deficiency is a major factor in pathogenesis of their infants was further confirmed. Vitamin D supplementation during pregnancy and lactation for the mother and breastfeeding infants is recommended to prevent vitamin D deficiency and rickets and their serious complications.

**Keywords:** Rickets, Vitamin D deficiency, Hypocalcaemia, Rachitic Rosary.

## **INTRODUCTION**

### **Rickets due to maternal vitamin d deficiency**

The first report of rickets in Riyadh, a sunny city was, seen among breastfeeding infants mainly in the first year of life, with a mean age of ten months.(Elidrissy andTaha,1980) Although congenital rickets has been reported before (Moncrieff M and Fadahunsi TO, 1974; Anatoliotaki M et al ,2003) the youngest infant seen with clinical rickets in our series was two months old and presented with hypocalcemic convulsions associated with minimal bony changes. (Elidrissy and Taha, 1980) In that first report we postulated that maternal vitamin D deficiency plays a major role in pathogenesis of infantile rickets. We put this hypothesis into tract of proving first by finding that the mothers of rachitic infants were vitamin D deficient.

(Elidrissy and Sedrani, 1984) Further paired maternal and cord blood vitamin D status proved to be low.(Serinius et al., 1984; Elidrissy et al., 1983) This maternal association of rickets seems to be historical as in the statement of Glisson, who said about the onset of rickets:(rarely invade children before they are six months old.) He continued to state that: (it then gradually affects children till they are two and peaks after that). (Dunn and Francis, 1597-1677) Convinced with this notion and trying to prove further in another area, as part of a study of rickets in Almadinah region for the first time, we collected paired blood samples from 40 infants with rickets and their mothers to study the levels of parathormone(PTH) and vitamin D(25OHD). In this communication, we are presenting the results of this study together with related relevant

factors and reviewing the literature.

## PATIENTS AND METHODS

In the period of six months from October 2008 to March 2009, as part of a retrospective hospital based study in Medina Maternity and Children Hospital (MMCH) this study was carried out. MMCH is a 300 bed pediatric hospital, the main referral centre for the Medina region. In this period 136 cases of rickets were diagnosed clinically and biochemically, but for the sake of evaluating the vitamin D status of the breastfeeding mothers, pairs of rachitic infants and their mothers were selected to evaluate and compare their vitamin D status. Mothers after being informed about the diagnosis of their infants were approached to collect blood from both of them, accordingly only mothers who gave a consent were included. Blood samples were collected from 40 pairs of mothers and breast fed babies admitted to hospital with their mothers or seen in the clinic. The samples were separated and stored at -70 degrees centigrade for later analysis by radio immune assay. Radiology of the right wrist was done for all infants to confirm the status of rickets being active or healed.

## RESULTS

Out of 40 samples of blood the results were available for 38 pairs. The cases were separated into two groups by finding radiological evidence of activity or healing together with the level of alkaline phosphatase where 400 units was taken as upper limit of normal. The biochemical results in the two groups of active and healed rickets are shown in the table 1. Calcium, phosphorus and 25 hydroxy-cholecalciferol (25OHD) were significantly low in active rickets compared to healed rickets, whereas alkaline phosphatase and PTH were significantly high in active rickets compared to healed rickets. The 25OHD level in children with active rickets and their mothers is shown in Figure 1 as chart; the mean level in infants with active rickets and their mothers was 10.5ng/ml and 12.1ng /ml and that of healed rickets and their mothers was 53.6 and 19. ng/ml respectively with a P value of 0.0393 which is significant. The mean PTH in active rickets was 197.9 pg/ml and in healed rickets 49.2 pg/ml. In the mothers it was 118.03 pg/ml in mothers of active rickets and 89.74 pg/ml in mothers of healed rickets as shown in figure 2.

## DISCUSSION

In our first report of rickets in Saudi Arabia, a sunny

country, a hypothesis that maternal vitamin D deficiency is a major factor in its pathogenesis was suggested. (Elidrisy and Taha, 1980) In a trial to prove this hypothesis 25-hydroxyvitamin D (25OHD) levels were found to be low in mothers of the rachitic infants (Elidrisy and Sedrani, 1984). We measured the vitamin D levels in 119 pregnant women at term and in their newborn babies. Concentrations of 25-OHD were below 4 ng/ml in 30 of 119 maternal sera (25%), in 11 of which they were undetectable. The median concentration of 25-OHD was 5.7 ng/ml, which was comparable to that found in Asian vegetarian women at term in London. Fifty of 119 (42%) cord samples had undetectable 25-OHD, and a total of 81 samples had 25-OHD concentrations of less than 4ng/ml. Despite the low 25-OHD concentrations cord blood had calcium concentrations higher than those in maternal blood, while serum albumin concentration was similar in maternal and cord samples. (Serinius et al., 1984) We further confirmed the low levels of vitamin D in pregnant mothers. (Belton et al., 1982) Interestingly another study from our group confirmed the low 25OHD in maternal and cord blood, but they followed the infants after a week and demonstrated a drop in their calcium level (Taha et al., 1984). These studies from Riyadh confirmed beyond doubt a major role of maternal vitamin D deficiency in pathogenesis of rickets in their infants. We are discussing in the coming pages the maternity-fetal transplacental metabolism of calcium and vitamin D and related metabolites with an objective of using it in preventing rickets and the associated serious complications namely hypocalcemic convulsions, cardiomyopathy, myelofibrosis, anemia etc.

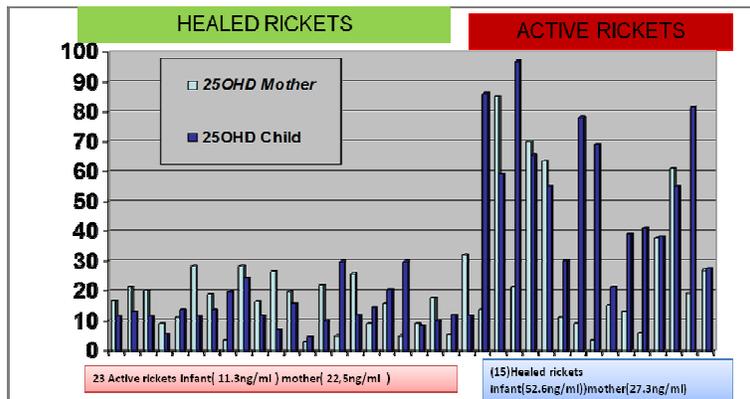
### Feto-maternal micronutrients metabolism

Calcium is a major component of the skeleton and there is great demand of it during pregnancy. The feto-maternal calcium metabolism and its relation to maternal vitamin is discussed to understand its effect on the fetus. Kovacs has reported this by stating that, during pregnancy and lactation, mothers require significant amounts of calcium to pass on to the developing fetus and suckling neonate, respectively. Given the dependence of adult calcium concentrations and bone metabolism on vitamin D, one might anticipate that vitamin D sufficiency would be even more critical during pregnancy and lactation. However, maternal adaptations during pregnancy and lactation and fetal adaptations provide the necessary calcium relatively independent of vitamin D status. It is the vitamin D-deficient or insufficient neonate who is at risk of problems, including hypocalcemia and rickets. Due to poor penetration of vitamin D and 25-OHD into milk, exclusively breastfed infants are at higher risk of

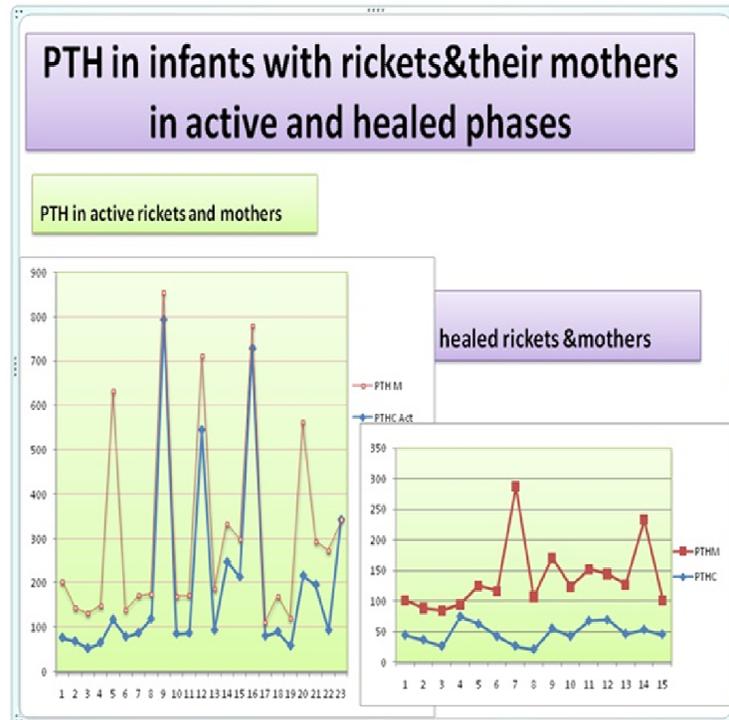
**Table 1.** Biochemical results in active and healed rickets

State of rickets	S calcium mmol/l	S phosphorous Mmol/l	ALP lu	PTH Pg/ml	25OHD Ng/ml
Active rickets	2.06	1.04	1148.0	199.86	13.9
Healed rickets	2.34	1.70	373.08	60.53	44.23
P value	0.0001	0.0001	<0.0001	0.0021	0.0393
results significance	Ext sig	Ext sig	Ext sig	V sig	sig

**Paired 25OHD levels in infants & mothers with active & healed Rickets**



**Figure 1.** Paired 25OHD levels in active and healed rickets in infants their mothers.



**Figure 2.** Paired PTH levels in Active rickets and their mothers

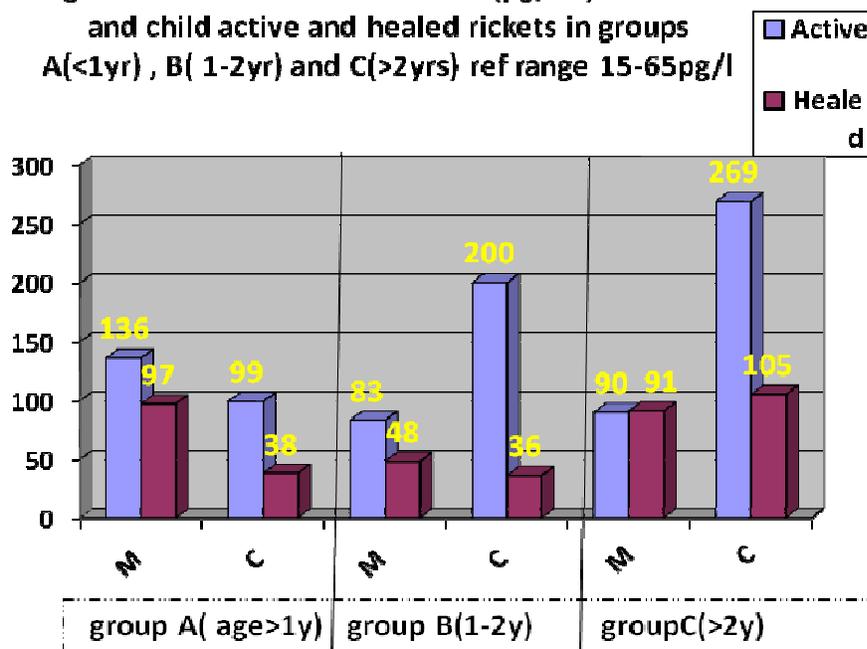
vitamin D deficiency than are formula-fed infants. (Kovacs, 2008) Here we record that 96% of our patients in this study and previously are breast fed. (Elidrisy and Taha, 1980; Elidrisy and Sedrani, 1984) Dosing recommendations for women during pregnancy and lactation might be best directed towards ensuring that the neonate is vitamin D-sufficient and that this sufficiency is maintained during infancy and beyond. A dose of vitamin D that provides 25-OHD sufficiency in the mother during pregnancy should provide normal cord blood concentrations of 25-OHD. Delvin et al., reported that 1,25-dihydroxyvitamin D appear to be present in the placenta suggesting that the placenta may be a target for vitamin D action. Developmental changes in vitamin D metabolism and action have been documented in the neonate as well as in the mother and fetus. Clinical studies indicate that adequate vitamin D intake is important during pregnancy. Administration of vitamin D or its metabolites appear to be useful in the treatment of neonatal disorders. After 31 weeks of gestation, calcium, magnesium, and inorganic phosphate cross the placental barrier against a concentration gradient. The fetus depends on the maternal supply for 25-hydroxyvitamin D and 24,25 dihydroxyvitamin D the fetoplacental unit synthesizes 1,25-dihydroxyvitamin D according to fetal needs (Delvin et al., 1982). During pregnancy maternal serum concentrations of 25 hydroxyvitamin D (25OHD) correlate with dietary vitamin D intake. Maternal serum concentrations of 1,25-dihydroxyvitamin D, the hormonal circulating and active form of vitamin D are elevated during pregnancy, being synthesized mainly by the deciduous cells of the placenta and allows for increased calcium absorption. The fetus is entirely dependent on the mother for its supply of 25-OHD which is believed to cross easily through the placenta. Vitamin D deficiency during pregnancy affects the fetus and the newborn. Birth weight is decreased, bone mineralization is impaired and neonatal hypocalcemia is frequent. In countries where dairy products are not routinely supplemented with vitamin D, maternal vitamin D supplementation during pregnancy is necessary. (Salle et al., 2002) We did not find a difference in birth weight between vitamin D sufficient or deficient mothers. Delvin et al., demonstrated the importance of providing adequate maternal vitamin D stores to ensure better prenatal handling of calcium, stressing that this is of particular importance for populations at risk for hypovitaminosis D. (Delvin et al., 1986) After reviewing many articles Specker found increased intestinal calcium absorption during pregnancy to meet fetal calcium demands. In cases of severe maternal vitamin D deficiency, serum PTH concentrations are increased, 1,25 (OH)<sub>2</sub>D concentrations are decreased, and osteomalacia may occur. Observational studies and vitamin D

supplementation trials among pregnant women at high risk of vitamin D deficiency showed improved neonatal handling of calcium with improved maternal vitamin D status. Results concerning the effects of vitamin D on maternal weight gain and fetal growth in these high-risk populations were conflicting and inconclusive. There is no evidence to indicate a beneficial effect of vitamin D intakes during pregnancy above amounts routinely required to prevent vitamin D deficiency among non pregnant women. (Specker, 2004) In a recent study Specker further stated that during pregnancy, maternal and fetal Ca demands are met through increased intestinal Ca absorption. Increased Ca absorption may be more dependent on estrogen's up-regulation of Ca transport genes than on vitamin D status. Numerous studies, however, have found that severe vitamin D deficiency with secondary hyperparathyroidism during pregnancy leads to abnormal Ca homeostasis in the neonate. Some, but not all, studies of maternal vitamin D supplementation during pregnancy find a greater birth weight among infants of mothers with adequate vitamin D status, this agrees with our finding. (Specker, 2012) Bruns and Bruns stated that, during pregnancy, the concentrations of 1,25-dihydroxyvitamin D in maternal serum increase in parallel with the increased need to absorb dietary calcium. 1,25-Dihydroxyvitamin D is produced in the fetoplacental unit as well as in the maternal kidneys. Receptors for 1, 25-dihydroxyvitamin D appear to be present in the placenta suggesting that the placenta may be a target for vitamin D action. Developmental changes in vitamin D metabolism and action have been documented in the neonate as well as in the mother and fetus. Clinical studies indicate that adequate vitamin D intake is important during pregnancy. Administration of vitamin D or its metabolites appears to be useful in the treatment of neonatal disorders. (Bruns and Bruns, 1983) Simmonds found that parathyroid hormone (PTH) and PTH-related protein (PTHrP) play complementary and overlapping roles in regulating fetal mineral homeostasis. PTHrP is expressed within the growth plate, directs endochondral bone formation, and determines the fate of chondrocytes before bone formation can be initiated. It is expressed in placenta and is present at high levels in the fetal circulation. PTH also stimulates placental calcium transfer. (Simmonds and Kovacs, 2010) Pitkin et al in an earlier report discussed calcium homeostasis describing it as a complex process involving calcium, and other ions, and three calcitropic hormones namely, parathyroid hormone, calcitonin, and 1,25-dihydroxyvitamin D<sub>3</sub>. The principal maternal adjustment during pregnancy is an increasing parathyroid hormone secretion which maintains the serum calcium concentration in the face of a falling albumin level, an expanding extracellular

fluid volume, an increasing renal excretion, and placental calcium transfer. The placenta transports calcium ions actively, making the fetus hypercalcemic relative to its mother, which in turn stimulates calcitonin release and perhaps suppresses parathyroid hormone secretion by the fetus. A unique extra renal system for 1 alpha-hydroxylation of 25-hydroxyvitamin D<sub>3</sub> exists in the placenta and/or deciduous, providing a source of 1, 25-dihydroxyvitamin D<sub>3</sub> for the fetus. With the abrupt cessation of the placental source of calcium at birth, the neonate's serum calcium level falls for 24 to 48 hours, then stabilizes and rises slightly. (Pitkin, 1985) The findings from the above studies stress on the active transplacental calcium transport which is independent on vitamin D level per se. This leads to normal intrauterine bone calcification of the fetus regardless of vitamin D level. It is only when postpartum calcium absorption is impaired due to lack of vitamin D in the breast milk that problems start. In spite of the high incidence of maternal vitamin D deficiency in our region we did not come across cases of congenital rickets presenting with obvious bony changes at birth and was not reported by others either, which is in support of the transplacental calcium pump independent of maternal vitamin D level. This supports our original hypothesis that although maternal vitamin D deficiency is prevalent during pregnancy, the real process of the pathogenesis of rickets in the newborn, starts only after birth. It is then when a cascade heralded by hypocalcemia followed by hyperparathyroidism in a trial to correct calcium by desorbing the bone stores, and leading to other biochemical abnormalities. In infants, the bones carry the major burden of changes obviously at the growing ends in addition to osteopenia. In maternal vitamin D deficiency which is common in our community from previous studies, (Serinius et al., 1984; Hatun et al., 2005) and evidence from this study of low 25OHD and high PTH both in mothers and their babies. (Figure 1-3) .The baby might be born with vitamin D deficiency associated with early biochemical rickets that manifest as hypocalcemic convulsions which is the commonest presentation of rickets during the early months of life, in our study being 33%, in infants below one year and up to 78% in infants below three months of age in a study from Turkey.(Hatun et al., 2005) Many other factors might play intrauterine to protect the unborn baby that is why florid rickets at birth is very rare. Maternal hyperparathyroidism might play a protective role for the fetus. It could be treated satisfactorily with high doses of supplemental calcium and vitamin D. Diabetes in pregnancy is associated with disturbed neonatal calcium homeostasis, perhaps due to chronic hypomagnesaemia. Dietary deficiency of calcium and/or vitamin D during gestation may lead to several adverse effects in the newborn infant. (Whitehead et

al., 1981). Another mechanism of meeting the increased need for calcium during pregnancy is the increased concentrations of 1,25-(OH)<sub>2</sub>D, enhancing intestinal absorption of this element. The simultaneous rise in calcitonin opposes the bone-desorbing activities of 1, 25-(OH)<sub>2</sub>D, thereby protecting the integrity of the maternal skeleton. Maternal calcium homeostasis is thus maintained under adverse situations, yet the requirements of the fetus are fulfilled (Whitehead M, Lange G et al., 1981). From the evidence of prenatal studies and from the data in this study we assume that rickets is prevented intrauterine by the calcium pump which is derived by PTH, but when born this protective support is no more available leading to a process starting by hypocalcemia followed by hypophosphatemia. As breast milk is low in vitamin D deficient mothers, absorption of calcium by the baby will be impaired and the hypocalcemia cannot be corrected. This hypocalcemia leads to stimulation of the parathyroid glands with the resultant hyperparathyroidism, which is observed in the three age groups of active rickets in figure 3. PTH is the guard responsible for maintaining normal calcium levels, as its activity is triggered by the drop in calcium. The mechanism of this correction is by approaching the calcium stores in the bones resulting in decalcification and softening of the bones and impairment of calcification of osteoclasts in the growing ends of bones in children giving rise to the classical features of rickets. This difference is noticed in infants below one year of age in our study who present by convulsions in 33% of cases and respiratory infections and gastrointestinal symptoms and features of rickets may not show, as stated by Glisson in his historical statement (Dunn and Glisson, 1597-1677). The PTH levels in the mothers of children with active rickets as shown in figure 2, was 135, 83 and 90 pg/ml in group A (age below 1 year, B (age between one and two years), and group C (age above two years), respectively (normal 15-65pg/ml). In children with active rickets groups A, B and C it was 99, 200 and 269 pg/ml respectively. The PTH levels are high in both mothers and children with active rickets. It is even higher in mothers of group A compared to other groups; this might be, it is still being under the stress of increased calcium demand of pregnancy and lactation. As regards to children with active rickets PTH levels are high all through but even higher with age suggesting activity of the disease where the older children present with florid and obvious features of rickets, that is to say, severe bow legs and knock-knees and swollen wrists and rachitic rosary etc. The 25OHD levels as shown in figure 1 in which the levels are low in both mother and child with active rickets and high in children with healed rickets most of them were on treatment. In the table 1 above the levels of calcium, phosphorus, alkaline phosphatase, PTH and 25OHD in active and healed rickets supports that.

**Fig3 Serum Parathormone level(pg/ml) in Mother and child active and healed rickets in groups A(<1yr) , B( 1-2yr) and C(>2yrs) ref range 15-65pg/l**



**Figure 3.** Serum Parathormone level (pg/ml) in Mother and child active and healed rickets in groups A (<1yr), B (1-2yr) and C (>2yrs) ref range 15-65pg

All the results are consistent with the different stages of the disease and activity. The most sensitive test is alkaline phosphatase which was consistently high in all age groups of rickets but drops with the start of the process of healing, so we are using its drop as the best evidence of healing of rickets. As regards to calcium it is low in early phase of rickets without radiological evidence of bony lesions. Further Mitchell and Juppner showed that Parathyroid hormone-related peptide plays an important role in transferring calcium across the placenta into the fetal circulation. In contrast, the factors controlling placental phosphate transport have not yet been explored, and numerous studies have indicated that maternal and childhood vitamin D deficiency continues to be a significant clinical concern. The molecular basis for mineral ion homeostasis in the fetus and child remains incompletely understood. More attention must be paid to identifying transplacental maternal, neonatal, and childhood vitamin D deficiency and associated calcium, phosphorus and PTH interrelations. (Mitchell and Juppner, 2010)

#### **Evidence of maternal vitamin D deficiency and neonatal effects**

We are reporting the available evidence from literature review, showing that maternal vitamin D deficiency is the corner stone in the development of rickets in her

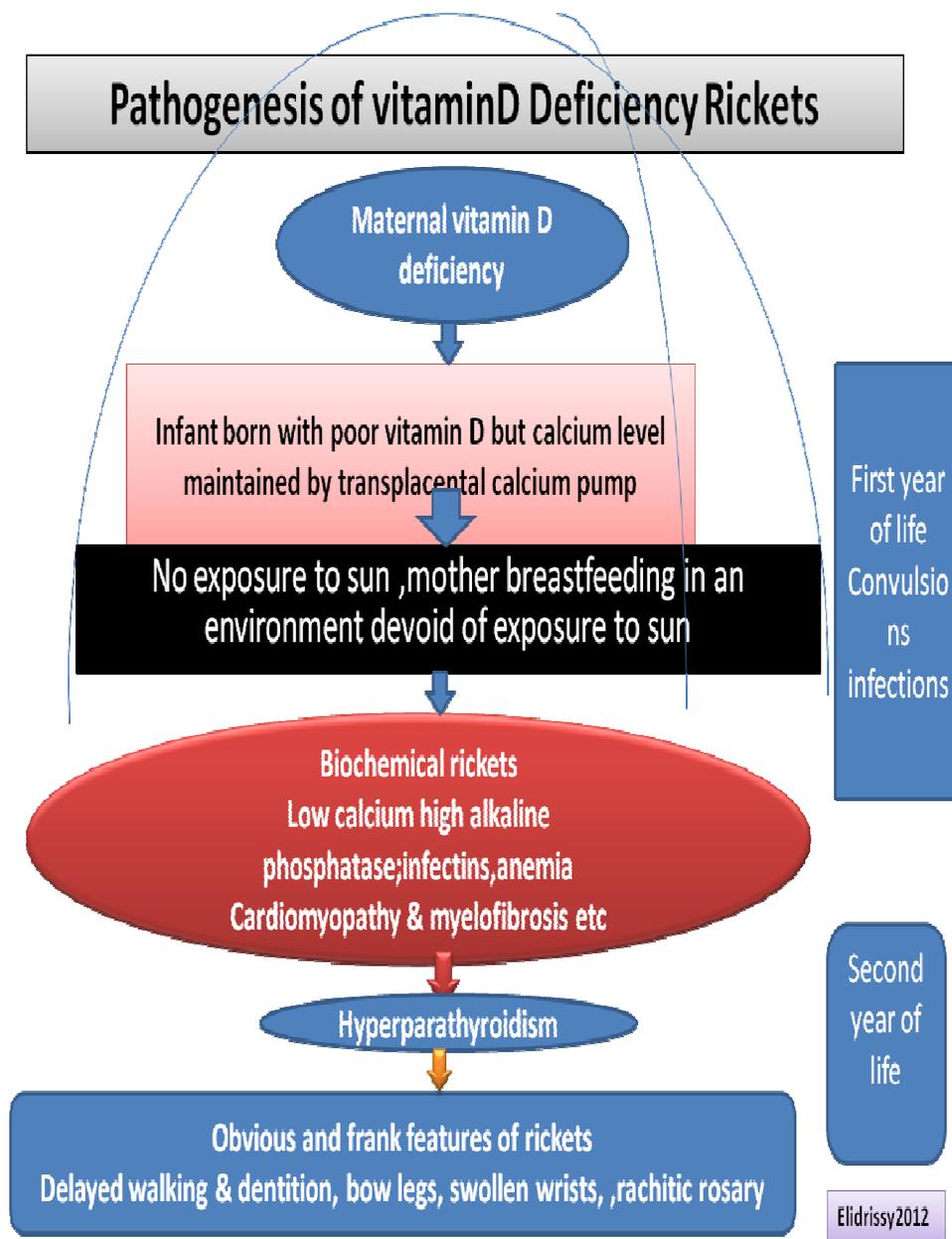
newborn infant. Hypocalcemia may not be symptomatic unless ionized calcium drops. This maternal factor in the pathogenesis of infantile rickets has been proved from many countries. From Australia, Nozza stated that 25 (81%) of mothers of infant having rickets had 25-hydroxyvitaminD3 concentrations less than 25nmol/L, consistent with osteomalacia. (Nozza and Rodd, 2001) Also Pillow et al reported rickets in infants of vitamin D deficient immigrant mothers. (Pillow et al., 1995) From USA it was found that, among mostly blacks, vitamin D deficiency (<30 nmol/L), was found in 50% of mothers and 65% of their newborn infants, with a positive correlation between maternal and infant plasma 25-hydroxyvitamin D concentrations, indicating that maternal vitamin D deficiency may represent an important risk factor for the development of rickets in children (Lee et al., 2007). In Egypt maternal vitamin D deficiency is common in nursing mothers of infants diagnosed with rickets. Invariably mothers of infants presenting with hypocalcemia seizures have severe vitamin D deficiency (Salama and El-Sakka, 2010). In India exclusively breastfed infants and their mothers were found to be Vitamin D deficient. (Agarwal et al., 2010) In UK Holmes stated that, Vitamin D insufficiency is evident in pregnant Caucasian women living at 54-55 degrees N. Women reporting use of vitamin D-containing supplements had higher vitamin D status, however, vitamin D insufficiency was still

evident even in the face of supplement use. Given the potential consequences of hypovitaminosis D on health outcomes, vitamin D supplementation, perhaps at higher doses than currently available, was recommended to improve maternal vitamin D nutritive. (Holmes et al., 2009) In Turkey, eight infants who presented with hypocalcaemic seizures were subsequently found to have rickets and their mothers had osteomalacia. Neither mothers nor infants received vitamin D supplementation. Maternal vitamin D deficiency and non-supplementation in the infants were causes of rickets in these patients. (Orbak et al., 2007) Erdeve stated that congenital rickets is considered a rare disease entity in the newborn period. Hypocalcaemic seizure due to congenital rickets was reported, at the earliest at the end of the first month of life. A congenital rickets case presented unusually with seizure on the first day of life, and the continuing occurrence of the disease with serious consequences even at the beginning of life was emphasized by these authors from Turkey. (Erdeve et al., 2007) From Australia a report of a week old Asian presenting with neonatal hypocalcaemic seizures secondary to vitamin D deficiency. There have been a very low 25OHD levels in both vegetarian mother and exclusively breast fed infant. (30) In Emirates(UAE) Vitamin D deficiency (serum 25-hydroxyvitamin D <25 nmol/L (<10 ng/mL)) was identified in 92% of rachitic Arab children and 97% of their mothers compared with 22% of non-rachitic children and 52% of their mothers. There was a positive correlation between maternal and child vitamin D levels. They concluded that mothers of rachitic children should be investigated and treated for vitamin D deficiency. (Dawodu et al., 2005) From Rotterdam three Arabs were reported a Moroccan male, a Turkish female and a Sudanese male newborn who presented with hypocalcaemic seizures in the second week of life. The hypocalcaemia was caused by neonatal vitamin-D deficiency as a result of maternal vitamin-D deficiency during pregnancy (Dijkstra et al., 2005). In two years study from Turkey a total of 42 infants (27 boys and 15 girls) were diagnosed with vitamin D deficiency among infants of age below three months. The mean age of these infants at diagnosis was 60 +/- 19 d (range 32-112 days). The majority (78.7%) presented with seizures. No skeletal deformities were detected clinically, and radiological findings were subtle. All infants had low serum calcium levels but serum phosphorous levels varied. Serum 25-hydroxyvitamin D levels in those measured (29 infants and 15 mothers) were <37.5 nmol/L (normal>50nmol/L). Most infants (83%) were exclusively breast-fed without supplemental vitamin D, and none of the mothers were supplemented with vitamin D during pregnancy. (Hatun et al., 2005) These cases were reported from different parts of the world mostly of dark skin but Caucasians were not immune. They all presented with

a state of vitamin D deficiency in the mothers during pregnancy or lactation. Their infants mostly breast fed and mostly presented with hypocalcaemic convulsions. Vitamin D deficiency is the common factor and breastfeeding supplied the babies with everything they need except vitamin D the mothers being deficient.

In conclusion the evidence from our original studies (Elidriessy and Taha 1980; Elidriessy et al., 1984; Serinus et al., 1984; Elidriessy et al., 1983) and others from the region; (Pillow et al., 1995) and this study have shown the correlation between low levels of 25OHD in the mothers and their rachitic infants. Many studies also have shown a correlation between low cord blood and maternal blood. These findings indicate the birth of a vitamin D deficient infant with normal calcium at birth. It is also an important issue that congenital rickets with features of rickets were seen only very rarely in situations of severe maternal calcium depletion.

**Congenital rickets** developed when maternal bone mineral and vitamin D stores had been completely exhausted as stated by Moncrieff in his original report of true congenital rickets in an Asian immigrant mother with osteomalacia. A low birth weight female baby showed at birth widely separated sutures, large fontanel, soft skull bones and easily dented (craniotabes) but no swelling in wrists or ankles and rib ends seemed enlarged but X-ray wrist was typical of active rickets. Biochemical testing showed low calcium and high alkaline phosphatase and Low 25OHD. This is the first reported case showing evidence of true congenital rickets at birth. (Moncrieff and Fadahunsi, 1974) Another case from a Greek island whose mother was completely secluded from day light. (Anatoliotaki et al., 1997) Further Mohaprata reported a term baby born to a mother with osteomalacia, and presented at birth with signs of florid rickets which was confirmed biochemically. (Mohapatra et al., 2003). The others who presented with hypocalcaemia only can be considered as biochemical rickets which starts after a week or so and there is no clinical or radiological evidence of rickets. (Serinius et al., 1984) Blond reported a newborn that showed typical signs of rickets at birth craniotabes and severe hypocalcaemia. The diagnosis of fetal rickets was confirmed by radiography. Maternal deficiency was revealed in this Moroccan mother who had suffered low back pain and parasthesia for several months during pregnancy (Blond et al., 2003). All these cases of true congenital rickets were having clinical and biochemical features of rickets at birth. The ones who present with hypocalcaemia in the first week or month can be considered occult congenital rickets, whose mothers are usually vitamin D deficient but not having osteomalacia. Why true congenital rickets is rare? From the cases reported with clinical features of rickets the evidence proves that true congenital rickets



**Figure 4.** Algorithm explaining the pathogenesis of rickets in breastfed infants and the impact of maternal deficiency

will be seen only when there is severe maternal symptomatic osteomalacia or primary hypoparathyroidism leading to depletion of body calcium stores of the mother. As have been noticed in our previous studies, in situations of maternal vitamin D deficiency the babies are born with poor stores of calcium and due to cessation of transplacental calcium pump after birth, they are unable to absorb calcium from breast milk which is vitamin D deficient. This leads to the start of the cascade of hypocalcaemia followed by hyperparathyroidism that leads to

mobilization of calcium from bones for the sake of more needy and vital organs like heart and brain.

Full blown picture of clinical rickets will appear later on after birth depending on how severe is the lack of calcium at birth, never the less the situation will aggravate when the mother breast feed her infant, as shown in figure 4, which is modified from what was published by us before (Elidrissy, 1991) That almost all rachitic infants are breastfed from vitamin D deficient mothers aggravates the situation as regards to calcium metabolism but the protein calorie

nutritional status of the rachitic infants was found to be satisfactory in a previous study of ours (Elidrisy, 1991) and in this study to be reported. The breast milk content of vitamin D in vitamin D deficient mother is obviously low if not absent. These rachitic factors include dwelling being flats in high buildings, customs of mothers usually staying indoors avoiding the too hot sun and going out only by night, the type of dress is not the sole factor, as they do not go out by day. Vitamin D deficiency in sunny countries is multi-factorial and is widely spread and is likely to increase with increased urbanization with high buildings without play areas or open spaces. This reminds us of the statement of Hutchinson about London (Dunn and Hutchison, 1871-1960).

## CONCLUSION

With these multi-factorial vitamin D deficiency in mothers and their infants associated with a fast growing high buildings as the only available residence it is difficult to give advice for prevention of vitamin D deficiency other than vitamin D supplementation to all pregnant mothers with 1000 to 2000 units of vitamin D3 in tablet form, starting in the second trimester and to be continued during lactation. As for breast feeding infants 400 units of vitamin D3 in form of drops daily up to two years of age, although its adequacy is questionable and further studies are required.

Historical closing remarks by Sir Hutchison (1871-1960) the author of clinical Methods

I want to close by statement of Sir Hutchison in early 20<sup>th</sup> century before discovery of vitamin D, Rickets is increasing because women's work ... in many of the large industrial towns rickets is extremely prevalent, for the reason that women to go to work in the factories, and their children are left at home badly looked after and improperly fed. A third factor in the production of rickets is found in the tendency for the population to be crowded together in large cities ... Now so potent are these factors ... that in many towns more than half of the children seen in the outpatient room exhibit the disease in a more or less marked degree. So the dictum ... still holds good that 'rickets is the most common, and, in its indirect results, the most fatal of all the diseases which peculiarly affect children' (Dunn and Robert, 1871-1960)

In the beginning of 21<sup>st</sup> century rickets is prevalent as it was before discovery of vitamin D I feel after thirty years of struggling to prevent rickets, in developing countries we are seeing more of high racy buildings without play areas for children to grow healthy by playing in the sunshine.

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