

A REVIEW OF VITAMIN D DEFICIENCY DURING PREGNANCY: WHO IS AFFECTED?

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ABSTRACT

Objectives. Vitamin D deficiencies have been documented in several populations, including aboriginal Canadians from isolated northern communities. Such deficiencies can impact the health of both the mother and her infant. This review was performed to determine how widespread vitamin D deficiency is during pregnancy.

Study design. Electronic literature search.

Methods. A Medline search was conducted using the Mesh terms "pregnancy" and "vitamin D". Those studies meeting the inclusion criteria were reviewed.

Results. 35 of 76 studies reported deficient mean, or median, concentrations of 25(OH)D. Low concentrations were reported among different ethnic groups around the world. In addition, deficient concentrations were identified in 3 northern First Nations communities in Manitoba.

Conclusions. Such deficiencies are of concern, as the developing fetus acquires its 25(OH)D across the placenta and may influence infant health. Future research is required to resolve the discourse surrounding ambiguous threshold values for vitamin D deficiencies and insufficiencies and to identify effective strategies to improve the vitamin D status of expectant women. Vitamin D supplementation may be necessary for many women during pregnancy, especially those in northern regions where endogenous synthesis may be constrained.

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Keywords: vitamin D, vitamin D deficiency, review, pregnancy

INTRODUCTION

Vitamin D deficiencies can result from inadequate cutaneous synthesis, limited dietary intake of vitamin D, or vitamin D pathway impairment (1). The extent of such deficiencies is

unknown, but have been documented in several populations, including Asian immigrants to northern Europe, dark skinned individuals, and the institutionalized (2-7). Recent research further confirms that vitamin D deficiency also occurs among women during pregnancy (8-

10). Such deficiencies may lead to rickets, hypocalcemia, delayed ossification and abnormal enamel formation in children, and osteoporosis, osteomalacia and bone fractures in adults (6,11,12), in addition to diminished host immune responses (13).

The lower limit of normal for 25(OH)D is controversial, with suggested values in the literature ranging from 15 to 40 nmol/L (10,14-18). Concentrations <40 nmol/L have been associated with insufficiency (14) and deficiency (15,18), while levels <25 nmol/L are believed to equate with rickets, or osteomalacia (15,18). However, concentrations exceeding 80 to 100 nmol/L have specific advocates (14,19).

Relying on reported nutritional intakes to infer 25(OH)D adequacy is often problematic and does not give insight into actual circulating levels (7,20,21). Therefore, assessing dietary intakes may not be the best predictor of vitamin D status. Rather, serum analysis continues to serve as a reliable method (20).

Specific references to vitamin D deficiency and its sequelae have been cited among certain populations in northern Manitoba, specifically those First Nations communities in the Island Lakes region of the province (8,22-24). These studies identified clinical vitamin D deficiency, or dietary inadequacies of vitamin D, among northern aboriginal persons. Knowing that such vitamin D deficits have been identified in northern Canada, it is also important to establish whether they exist in other regions of Canada and around the globe.

This review was performed to determine how widespread vitamin D deficiency is during pregnancy, using a cutoff level of ≤ 35 nmol/L, the lower threshold of normal for serum vitamin D (25(OH)D) used in Manitoba.

STUDY DESIGN

Data Sources

A search of the Medline database was conducted from 1966 to 2002, inclusive, to identify studies reporting deficient maternal concentrations of 25(OH)D. The Mesh search terms used included "pregnancy" and "vitamin D".

Study Selection

A criterion for inclusion is that the study reported mean, or median, concentrations of 25(OH)D for healthy women during pregnancy, at term, delivery, or shortly thereafter. No language restrictions were enforced. Data from a recent unpublished study of vitamin D deficiency among expectant women from three northern Manitoba First Nations communities were also reviewed.

METHODS

Data Extraction

Studies were scrutinized to identify populations with mean, or median, maternal concentrations ≤ 35 nmol/L. Studies reporting concentrations in ng/ml were converted to nmol/L (1 nmol/L = 2.67 ng/ml). This cut-off was selected as it represents the lower limit of normal for 25(OH)D analysis in Manitoba. This threshold is based upon reference range values used by the Mayo Clinic Laboratories in Minnesota to signify the lower limit of normal based on their HPLC test (8). Prior to the late 1990s, all 25(OH)D assays in Manitoba were sent to the Mayo Clinic Laboratories for analysis. When analysis for 25(OH)D began in Manitoba using the INCSTAR kit, these same reference ranges were adopted.

RESULTS

A total of 76 studies were identified, thirty-five reporting mean, or median, maternal concentrations ≤ 35 nmol/L. Low 25(OH)D levels were not restricted to specific global regions. In fact, low concentrations were re-

ported among different ethnic groups in many regions (Table I), including North America, Europe, the United Kingdom, Africa, the Middle East and Asia. Details of the studies including population and mean, or median, 25(OH)D levels appear in table II.

Table I. Number of studies reporting deficiencies by geographic region.

Geographic Region	Number of Studies
North America (8,25)	2
Europe (2-4,10,26-34)	13
United Kingdom (35-44)	10
Africa (45,46)	2
Middle East (47-50)	4
Asia (9, 51-53)	4

Table II. Included Studies Reporting 25(OH)D in the Deficient Range (<35nmol/L)

Included Study	Population and Details	25(OH)D (Mean \pm SD, or Median)
Goswami R et al (2000)(9)	Dehli, India, Pregnancy Summer (n=29)	21.9 \pm 10.73 nmol/L
Koenig J & Elmadfa (2000)(10)	Austria, Pregnancy (n=231)	17.0 \pm 33.1 nmol/L
Smith PJ (2000)(8)	Canadian First Nations, Pregnancy Garden Hill, Manitoba (n=32) St. Theresa Point, Manitoba (n=35) Norway House, Manitoba (n=37)	18 nmol/L median (range <15-59) 21 nmol/L median (range <15-63) 24 nmol/L median (range <15-60)
Feleke Y et al (1999)(45)	Addis Ababa, Ethiopian Pregnancy (n=31) August-September Group	25 nmol/L median (range 17-46)
Brunvand L et al (1998)(51)	Karachi, Pakistan Primiparous women, Delivery (n=80)	19 nmol/L median (range 11-27)
Namgung R et al (1998)(52)	South Korean, Pregnancy Winter Season (n=34)	24 \pm 13 nmol/L
Ardawi MS et al (1997)(49)	Saudi Arabia Third Trimester (n=40) Term	33 \pm 8 nmol/L 35 \pm 11 nmol/L
Sanchez PA et al (1997)(46)	Maiduguri, Nigeria First Trimester (n=10)	25.87 \pm 8.62 nmol/L
Brunvand L et al (1996)(3)	Oslo, Norway Pakistani Immigrants – Delivery (n=30)	14 nmol/L median (range <5-31)
Bruinse HW & van den Berg (1995)(26)	Netherlands (n=70) – Late Winter, End of Pregnancy	32 \pm 9 nmol/L
Henrikson C et al (1995)(4)	Oslo, Norway Pakistani Immigrants – Second Trimester (n=38)	19 nmol/L median (range 15-25)
Brunvand L & Haug (1993)(2)	Oslo, Norway Pakistani Immigrants Delivery (n=30)	15.1 nmol/L

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Included Study	Population and Details	25(OH)D (Mean \pm SD, or Median)
Zeghoud F et al (1991)(27)	France –Delivery	
	Lyon: May (n=12)	20.3 \pm 8.8 nmol/L
	June (n=6)	33.9 \pm 16.6 nmol/L
	Chambery: May (n=5)	27.2 \pm 14.4 nmol/L
	June (n=6)	34.7 \pm 22.2 nmol/L
	Nice: May (n=5)	33.6 \pm 12.5 nmol/L
	June (n=9)	31.5 \pm 16.8 nmol/L
Zeghoud F et al (1988)(28)	France	
	Placebo Group	
	March (n=4): 6 months	27.5 \pm 9.6 nmol/L
	Delivery	20.0 \pm 10.1 nmol/L
	April (n=5): 6 months	27.8 \pm 5.4 nmol/L
	Delivery	21.4 \pm 3.0 nmol/L
	100000 IU at 6 month	
	April (n=5): 6 month (pre)	31.5 \pm 17.3 nmol/L
	100000 IU at 7 months	
	March (n=2): 6 months	21.4 \pm 11.2 nmol/L
Term	34.7 \pm 7.5 nmol/L	
April (n=7): 6 months	26.7 \pm 11.3 nmol/L	
Okonofua F et al (1987)(35)	London	
	Asians	
	First Trimester (n=11)	6.2 nmol/L median (range <5-8.2)
	Second Trimester (n=11)	12.5 nmol/L median (range <5-18.7)
	Third Trimester (n=10)	7.8 nmol/L median (range <5-28.5)
	Term (n=11)	13.1 nmol/L median
	Caucasian	
	First Trimester (n=18)	21.7 nmol/L median (range 11.0-57.2)
	Third Trimester (n=15)	26.5 nmol/L median (range 5.0-39.5)
	Term (n=12)	23.5 nmol/L median (range 14.5-46.2)
Delvin EE et al (1986)(29)	Lyon, France	
	Control Group (n=20)	
	Third Trimester	29.4 \pm 47.8 nmol/L
	Delivery	34.7 \pm 95.5 nmol/L
Kuoppala T et al (1986)(30)	Tampere, Finland	
	Spring-Delivery (n=18)	26.0 \pm 13.0 nmol/L
Mallet E et al (1986)(31)	France, Winter-Term	
	Control Group (n=29)	9.4 \pm 4.9 nmol/L
	1000 IU daily 3rd Trimester (n=21)	25.3 \pm 7.7 nmol/L
	200000 IU 7th Month (n=27)	26.0 \pm 6.4 nmol/L
Kuoppala T et al (1984)(32)	Tampere, Finland	
	Delivery (n=18)	13.8 \pm 9.8 nmol/L
Markestad T et al (1984)(47)	Benghazi, Libya	
	Delivery (n=34)	34 nmol/L median (range 13-75)
Serenius F et al (1984)(48)	Riyadh, Saudi Arabia	
	Measured at Term	
	Supplemented during pregnancy (n=73)	19.81 nmol/L median
	Unsupplemented (n=43)	14.02 nmol/L median
	Supplemented during Third pregnancy (n=53)	19.86 nmol/L median
	Unsupplemented (n=59)	15.49 nmol/L median
Ong SP et al (1983)(36)	Leeds, England	
	Pregnancy, November-January	
	All (n=46)	11.53 \pm 7.05 nmol/L
	Pakistani (n=17)	10.15 \pm 6.01 nmol/L
	Indian (n=19)	10.79 \pm 8.22 nmol/L
	Bangladeshi (n=10)	13.94 \pm 6.59 nmol/L

Table II continues to the next page

Table II continues from the previous page

Included Study	Population and Details	25(OH)D (Mean \pm SD, or Median)
Reddy GS et al (1983)(25)	Montreal, Canada Twin Pregnancy (n=27), Delivery	29.4 \pm 18.6 nmol/L
Gupta MM et al (1982)(53)	Pune, India March-October-Delivery (n=60)	31.32 \pm 17.68 nmol/L
Brooke OG et al (1981)(37)	London, Third Trimester Indian (n=65) Pakistani (n=19) East African (n=17) Bangladeshi (n=7) Nov-January (n=43) February-April (n=26) May-July (n=23) August-October (n=13)	18 \pm 21 nmol/L 10 \pm 12 nmol/L 21 \pm 26 nmol/L 32 \pm 15 nmol/L 19.8 \pm 23.0 nmol/L 18.8 \pm 18.7 nmol/L 18.9 \pm 14.7 nmol/L 28.0 \pm 20.0 nmol/L
Maxwell JD et al (1981)(38)	London, Asians Third Trimester Treatment Group (n=59) Control Group (n=67)	20.2 nmol/L 20.0 nmol/L
Whitehead JD et al (1981)(39)	London, Caucasian May-July 30-32 weeks (n=11) 36-40 weeks (term)(n=11)	21.4 nmol/L 20.4 nmol/L
Brooke OG et al (1980)(40)	London Placebo Group (n=67)-Term	16.2 \pm 22.1 nmol/L
Brown IRF et al (1980)(41)	London, Indian & Pakistani All pre-28 weeks (n=113) Placebo Group-Term (n=53)	20.1 \pm 20.2 nmol/L 16.0 \pm 19.7 nmol/L
Cockburn F et al (1980)(42)	Edinborough Placebo Group-24weeks (n=82) Placebo Group-Delivery (n=84)	32.5 nmol/L 32.5 nmol/L
Kokot F et al (1980)(33)	Poland-Winter-Spring Third Trimester (n=36)	24.83 \pm 13.3 nmol/L
Biale Y et al (1979)(50)	Beersheva, Israel Bedouin during Labour (n=8)	20.72 \pm 19.97 nmol/L
Heckmatt JZ et al (1979)(43)	Leeds, Asians, September-October, Delivery (n=43)	14.2 \pm 20.3 nmol/L
Paunier L et al (1978)(34)	Switzerland, Delivery January-February (n=16) Control Group 500 IU vitamin D in multivitamin (n=16)	24.3 \pm 16.0 nmol/L 29.6 \pm 13.9 nmol/L
Dent CE & Gupta (1975)(44)	London, July-August Asians (n=39) at Delivery Vegetarian Asian 10-26 weeks 28-32 weeks 33-40 weeks Non-vegetarian Asian 10-26 weeks 28-32 weeks 33-40 weeks West Indian (n=3) 10-26 weeks 28-32 weeks	20.3 \pm 13.3 nmol/L 24.0 \pm 41.0 nmol/L 24.5 \pm 30.7 nmol/L 19.6 \pm 21.8 nmol/L 28.5 \pm 23.5 nmol/L 27.0 \pm 17.1 nmol/L 26.0 \pm 12.8 nmol/L 30.3 \pm 7.4 nmol/L 28.0 \pm 13.9 nmol/L

DISCUSSION

Vitamin D deficiency among expectant women is not limited to specific ethnic groups or regions, but is prevalent worldwide. While many studies involved Asian immigrants and those of Asian extraction residing in northern Europe and the UK (2-4,36,37,43), low levels are exhibited by pregnant women from regions with ample sunshine. For instance, expectant mothers were found to have 25(OH)D concentrations at, or below, 25 nmol/L during summer in Delhi (9), at delivery in Pakistan (51), and in Addis Ababa, Ethiopia (45). Even mothers in southern France had low levels during May and June (27).

Low levels are not restricted to poor countries, but also to highly industrialized countries, more specifically disadvantaged subpopulations within those countries, such as aboriginal people in Canada. Their low socio-economic status (SES) and abandonment and lack of a traditional diet, along with the northern latitude, preclude proper attainment of vitamin D levels (54). This is evident in the communities of St. Theresa Point, Garden Hill, and Norway House, where median concentrations for 25(OH)D were below 25 nmol/L (8). Such widespread vitamin D deficiencies during pregnancy undoubtedly have health implications for both expectant mothers and their offspring. Similar deficits have also been reported among other northern Canadians, including First Nations and Inuit mothers in the Northwest Territories (55). These findings, along with those of a recent Cochrane systematic review, highlight the need for vitamin D supplementation as a preventive strategy to combat vitamin D deficiencies, especially among

women residing in northern regions where endogenous synthesis is limited (56).

The majority of studies reporting values below 35 nmol/L were from Europe and the UK. However, much of the research was conducted in that region, increasing the probability of identifying those with existing deficiencies. It is possible that more women are deficient during pregnancy, but have yet to be identified because of limited research. It is also probable that some women in the excluded studies had low concentrations, but they were not identified as mean cohort values exceeded our threshold (55).

Assays for 25(OH)D are not routine medical tests and are often cost-prohibitive (57). This is probably a reason more research has not been conducted to determine the prevalence of vitamin D deficiencies worldwide.

While this review demonstrates that many have low concentrations, it also indicates that supplementation alone is not sufficient to produce maternal levels above 35 nmol/L (28,48). Mothers receiving 100,000 IU of vitamin D at 7 months gestation had a mean concentration just shy of 35 nmol/L at term (28), while mothers receiving differing supplementation strategies were found to have term levels below 25 nmol/L (49). Evidence also indicates that regular intake of multivitamins and fortified foods may not produce increases beyond the 40 nmol/L threshold (7,20).

Comparisons of 25(OH)D concentrations between published studies can be difficult, since laboratory techniques vary; for example, radioimmunoassay generally yields higher concentrations than high performance liquid chromatography (HPLC) (58). Whereas this is a limitation of this review, comparative data are nonetheless compelling.

Another limitation of this review is that it does not meet the scientific rigour of a formal systematic review, as the search strategy was limited and only one electronic database was searched. In addition, there was no formal attempt to search the grey literature.

Health care providers delivering ambulatory care to expectant mothers should be cognizant that mothers and developing fetuses may be at risk for insufficient 25(OH)D. In Canada, this is especially true for northern residents, including First Nations people, as latitude and less than nutritious diet may lead to deficiencies. This may also be true for those in southern regions of Canada, especially during winter (14), or those of low SES who are unable to secure foods naturally containing, or fortified with, vitamin D.

Recommendations have now surfaced for all expectant mothers with dark complexion, or limited sun exposure, to be routinely assessed for 25(OH)D during their pregnancies (6). This could arguably apply to aboriginal people residing in Canada's north. Future research needs

to identify those optimal concentrations that would provide maximum effectiveness in maternal, fetal and infant health (6).

CONCLUSIONS

Many expectant mothers have deficient 25(OH)D concentrations. This is of concern, as the developing fetus acquires its 25(OH)D across the placenta. Therefore, offspring of mothers with low levels will also have low concentrations, leaving them vulnerable to potential rickets, hypocalcemia and possible enamel defects. Such concerns over vitamin D insufficiencies and deficiencies are further heightened for residents of the north and, in particular, aboriginal people. Future epidemiological investigations are welcomed to resolve the ambiguity surrounding threshold concentrations for deficiency and to further document existing deficiencies. Clinical trials are needed to identify effective preventive strategies during pregnancy to achieve vitamin D adequacy.

REFERENCES

1. Combs GF. Vitamin D. The vitamins: fundamental aspects in nutrition and health. San Diego: Academic Press, 1998: 155-187.
2. Brunvand L, Haug E. Vitamin D deficiency amongst Pakistani women in Oslo. *Acta Obstet Gynecol Scand* 1993; 72(4):264-268.
3. Brunvand L, Henriksen C, Haug E. [Vitamin D deficiency among pregnant women from Pakistan. How best to prevent it?]. *Tidsskr Nor Laegeforen* 1996; 116(13): 1585-1587.
4. Henriksen C, Brunvand L, Stoltenberg C, Trygg K, Haug E, Pedersen JI. Diet and vitamin D status among pregnant Pakistani women in Oslo. *Eur J Clin Nutr* 1995; 49(3):211-218.
5. Goor Y, Rubinstein A. Vitamin D levels in dark-skinned people. *Isr J Med Sci* 1995; 31(4):237-238.
6. Grover SR, Morley R. Vitamin D deficiency in veiled or dark-skinned pregnant women. *Med J Aust* 2001; 175(5): 251-252.
7. Thomas MK, Lloyd-Jones DM, Thadhani RI, et al. Hypovitaminosis D in medical inpatients. *N Engl J Med* 1998; 338(12):777-783.
8. Smith PJ. Vitamin D deficiency in three northern Manitoba communities. PhD thesis. University of Manitoba, 2000.
9. Goswami R, Gupta N, Goswami D, Marwaha RK, Tandon N, Kochupillai N. Prevalence and significance of low 25-hydroxyvitamin D concentrations in healthy subjects in Delhi. *Am J Clin Nutr* 2000; 72(2):472-475.
10. Koenig J, Elmadfa I. Status of calcium and vitamin D of different population groups in Austria. *Int J Vitam Nutr Res* 2000; 70(5):214-220.
11. Utiger RD. The need for more vitamin D. *N Engl J Med* 1998; 338(12):828-829.
12. Specker BL. Do North American women need supplemental vitamin D during pregnancy or lactation? *Am J Clin Nutr* 1994; 59(2 Suppl):484S-490S.
13. Griffin MD, Xing N, Kumar R. Vitamin D and its Analogs as Regulators of Immune Activation and Antigen Presentation. *Annu Rev Nutr* 2003; 23:117-45.

14. Rucker D, Allan JA, Fick GH, Hanley DA. Vitamin D insufficiency in a population of healthy western Canadians. *CMAJ* 2002; 166(12):1517-1524.
15. Nozza JM, Rodda CP. Vitamin D deficiency in mothers of infants with rickets. *Med J Aust* 2001; 175(5):253-255.
16. Abrams SA. Nutritional rickets: an old disease returns. *Nutr Rev* 2002; 60(4):111-115.
17. O'Shea D, Carter GD. Hypovitaminosis D in medical inpatients. *N Engl J Med* 1998; 339(5):345-346.
18. Salle B, Glorieux F, Lapillone A. Vitamin D status in breastfed term babies. *Acta Paediatr* 1998; 87:726-727.
19. Zittermann A. Vitamin D in preventive medicine: are we ignoring the evidence? *Br J Nutr* 2003; 89(5):552-572.
20. Vieth R, Cole DE, Hawker GA, Trang HM, Rubin LA. Wintertime vitamin D insufficiency is common in young Canadian women, and their vitamin D intake does not prevent it. *Eur J Clin Nutr* 2001; 55(12):1091-1097.
21. Vieth R. Vitamin D supplementation, 25-hydroxyvitamin D concentrations, and safety. *Am J Clin Nutr* 1999; 69(5):842-856.
22. Lebrun JB, Moffatt ME, Mundy RJ, et al. Vitamin D deficiency in a Manitoba community. *Can J Public Health* 1993 Nov-Dec; 84(6):394-6.
23. Haworth JC. Rickets still affects Canadian children. *CMAJ* 1995 Sep 15; 153(6):740-1.
24. Haworth JC, Dilling LA. Vitamin-D-deficient rickets in Manitoba, 1972-84. *CMAJ* 1986 Feb 1; 134(3):237-41.
25. Reddy GS, Norman AW, Willis DM, 'et al.'. Regulation of vitamin D metabolism in normal human pregnancy. *J Clin Endocrinol Metab* 1983; 56(2):363-370.
26. Bruinse HW, van den Berg H. Changes of some vitamin levels during and after normal pregnancy. *Eur J Obstet Gynecol Reprod Biol* 1995; 61(1):31-37.
27. Zeghoud F, Thoulon JM, Gillet JY, Chabert P, Garabedian M. [Effects of sunlight exposure on vitamin D status in pregnant women in France]. *J Gynecol Obstet Biol Reprod (Paris)* 1991; 20(5):685-690.
28. Zeghoud F, Garabedian M, Jardel A, Bernard N, Melchior J. [Administration of a single dose of 100,000 U.I. of vitamin D3 in the pregnant woman in winter: The effect on blood calcium level of the newborn infant]. *J Gynecol Obstet Biol Reprod (Paris)* 1988; 17(8):1099-1105.
29. Delvin EE, Salle BL, Glorieux FH, Adeleine P, David LS. Vitamin D supplementation during pregnancy: effect on neonatal calcium homeostasis. *J Pediatr* 1986; 109(2):328-334.
30. Kuoppala T, Tuimala R, Parviainen M, Koskinen T, Alahouhala M. Serum levels of vitamin D metabolites, calcium, phosphorus, magnesium and alkaline phosphatase in Finnish women throughout pregnancy and in cord serum at delivery. *Hum Nutr Clin Nutr* 1986; 40(4):287-293.
31. Mallet E, Gugi B, Brunelle P, Henocq A, Basuyau JP, Lemeur H. Vitamin D supplementation in pregnancy: a controlled trial of two methods. *Obstet Gynecol* 1986; 68(3):300-304.
32. Kuoppala T, Tuimala R, Parviainen M, Koskinen T. Can the fetus regulate its calcium uptake? *Br J Obstet Gynaecol* 1984; 91(12):1192-1196.
33. Kokot F, Pietrek J, Cekanski A. Concentration of 25-hydroxyvitamin D (25-OH-D) in peripheral and uterine blood of pregnant women, in amniotic fluid and in the umbilical cord blood. *Acta Med Pol* 1980; 21(1):31-38.
34. Paunier L, Lacourt G, Pilloud P, Schlaeppi P, Sizonenko PC. 25-hydroxyvitamin D and calcium levels in maternal, cord and infant serum in relation to maternal vitamin D intake. *Helv Paediatr Acta* 1978; 33(2):95-103.
35. Okonofua F, Menon RK, Houlder S, et al. Calcium, vitamin D and parathyroid hormone relationships in pregnant Caucasian and Asian women and their neonates. *Ann Clin Biochem* 1987; 24 (Pt 1):22-28.
36. Ong SP, Ryley J, Bashir T, Macdonald HN. Nutrient intake and associated biochemical status of pregnant Asians in the United Kingdom. *Hum Nutr Appl Nutr* 1983; 37(1):23-29.
37. Brooke OG, Brown IR, Cleeve HJ, Sood A. Observations on the vitamin D state of pregnant Asian women in London. *Br J Obstet Gynaecol* 1981; 88(1):18-26.
38. Maxwell JD, Ang L, Brooke OG, Brown IR. Vitamin D supplements enhance weight gain and nutritional status in pregnant Asians. *Br J Obstet Gynaecol* 1981; 88(10):987-991.
39. Whitehead M, Lane G, Young O, et al. Interrelations of calcium-regulating hormones during normal pregnancy. *Br Med J (Clin Res Ed)* 1981; 283(6283):10-12.
40. Brooke OG, Brown IR, Bone CD, et al. Vitamin D supplements in pregnant Asian women: effects on calcium status and fetal growth. *Br Med J* 1980; 280(6216):751-754.
41. Brown IR, Brooke OG, Cleeve HJ. Changes in mineral metabolism in the human foetus and newborns associated with maternal vitamin D supplements [proceedings]. *Biochem Soc Trans* 1980; 8(1):136-137.
42. Cockburn F, Belton NR, Purvis RJ, et al. Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *Br Med J* 1980; 281(6232):11-14.
43. Heckmatt JZ, Peacock M, Davies AE, McMurray J, Isherwood DM. Plasma 25-hydroxyvitamin D in pregnant Asian women and their babies. *Lancet* 1979; 2(8142):546-548.
44. Dent CE, Gupta MM. Plasma 25-hydroxyvitamin-D-levels during pregnancy in Caucasians and in vegetarian and non-vegetarian Asians. *Lancet* 1975; 2(7944):1057-1060.
45. Feleke Y, Abdulkadir J, Mshana R, et al. Low levels of serum calcidiol in an African population compared to a North European population. *Eur J Endocrinol* 1999; 141(4):358-360.
46. Sanchez PA, Idrisa A, Bobzom DN, et al. Calcium and vitamin D status of pregnant teenagers in Maiduguri, Nigeria. *J Natl Med Assoc* 1997; 89(12):805-811.
47. Markestad T, Elzouki A, Legnain M, Ulstein M, Aksnes L. Serum concentrations of vitamin D metabolites in maternal and umbilical cord blood of Libyan and Norwegian women. *Hum Nutr Clin Nutr* 1984; 38(1):55-62.
48. Serenius F, Elidrisy AT, Dandona P. Vitamin D nutrition in pregnant women at term and in newly born babies in Saudi Arabia. *J Clin Pathol* 1984; 37(4):444-447.
49. Ardawi MS, Nasrat HA, BA'Aqueel HS. Calcium-regulating hormones and parathyroid hormone-related peptide in normal human pregnancy and postpartum: a longitudinal study. *Eur J Endocrinol* 1997; 137(4):402-409.

50. Biale Y, Shany S, Levi M, Shainkin-Kestenbaum R, Berlyne GM. 25 Hydroxycholecalciferol levels in Beduin women in labor and in cord blood of their infants. *Am J Clin Nutr* 1979; 32(12):2380-2382.
51. Brunvand L, Shah SS, Bergstrom S, Haug E. Vitamin D deficiency in pregnancy is not associated with obstructed labor: A study among Pakistani women in Karachi. *Acta Obstet Gynecol Scand* 1998; 77(3):303-306.
52. Namgung R, Tsang RC, Lee C, Han DG, Ho ML, Sierra RI. Low total body bone mineral content and high bone resorption in Korean winter-born versus summer-born newborn infants. *J Pediatr* 1998; 132(3 Pt 1):421-425.
53. Gupta MM, Kuppuswamy G, Subramanian AR. Transplacental transfer of 25-hydroxy-cholecalciferol. *Postgrad Med J* 1982; 58(681):408-410.
54. Moffatt ME. Current status of nutritional deficiencies in Canadian aboriginal people. *Can J Physiol Pharmacol* 1995; 73(6):754-758.
55. Waiters B, Godel JC, Basu TK. Perinatal vitamin D and calcium status of northern Canadian mothers and their newborn infants. *J Am Coll Nutr*. 1999; 18(2):122-126.
56. Mahomed K, Gulmezoglu AM. Vitamin D supplementation in pregnancy (Cochrane Review). In: *The Cochrane Library*, Issue 1, 2002.
57. Welch TR, Bergstrom WH, Tsang RC. Vitamin D-deficient rickets: the reemergence of a once-conquered disease. *J Pediatr* 2000; 137(2):143-145.
58. Gannage-Yared MH, Chemali R, Yaacoub N, Halaby G. Hypovitaminosis D in a sunny country: relation to lifestyle and bone markers. *J Bone Miner Res* 2000; 15(9): 1856-1862.

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