Reduced Fertility in Saudi Arabian Men with Low Vitamin D Levels

Maryam Sarwat
Gowher Nabi
Tajdar H. Khan
Faris Q. Alenzi

A high prevalence of vitamin D deficiency has been found in Saudi Arabia, which can be directly attributed to inadequate exposure of sunlight largely due to religious practices and lifestyle. The poor dietary intake of vitamin D further adds to this problem. Various researchers have proved vitamin D deficiency to be linked with increased incidences of cancer, diabetes, and autoimmune and cardiovascular diseases. Recently, scientists have found an association of vitamin D deficiency with reduced testosterone levels. This can be attributed to increasing incidences of male infertility in Saudi Arabia. The rising incidences of infertility in Saudi males can be attributed to their decreasing vitamin D levels. Taking adequate measures to overcome the vitamin D deficiency can improve their sexual vigor.

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- Diabetes Mellitus, Type 2
- Testosterone
- Vitamin D Deficiency
- Vitamin D Response Element

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Background

Vitamin D maintains calcium and phosphorus homeostasis and promotes bone mineralization [1]. If the serum 25-hydroxyvitamin D [25 (OH)D] concentration of a person is 50 nmol/L or above, it is considered as normal, and lower levels are considered as vitamin D deficiency [2–4]. The Saudi Arabian population largely suffers from vitamin D deficiency, and this problem has increased tremendously from the initial assessment done in 1983 [5]: from >50% [6,7] to 83.6% [8]. It is well-established that sunlight is the best source for the vitamin D synthesis in the human skin. Various factors such as type of skin, time of day and year, and weather conditions are important in vitamin D synthesis. The geographical location of a particular region also influences vitamin D synthesis. The Norwegian Institute for Air Research has devised a very interesting calculator [9] to calculate the duration of exposure required to produce 25 mcg (equivalent to 1000 International Units) of vitamin D. Further, Alsharani et al. [10] calculated that in the summer months, only 10–15 min of sun exposure from 9: 00 A.M. to 10: 30 A.M. and between 2: 00 P.M. to 3: 00 P.M. is sufficient for the required daily dose of vitamin D. This research has been done in the Riyadh region (Saudi Arabia). This useful vitamin can be obtained from several food sources, amongst which fish liver oil and fatty fishes are the best [11]. Beef liver, cheese, and egg yolks also provide this vitamin, but in small quantities. Another point of concern is that the Saudi population is not obtaining adequate vitamin D from dietary sources. Their daily dietary intake of vitamin D is a meagre one-tenth of that of the United States [12]. Fortified food is another important means for obtaining vitamin D. Surprisingly, in Saudi Arabia, only wheat and enriched treated flour are mandatorily fortified with vitamin D (at the concentration of 55.1 IU/100g (Saudi Standard of Fortification)), but the fortification levels are lower compared to other countries [13,14]. The Saudi Standard of Fortification has no rules to fortify other food items like milk, cheese, breakfast cereals, and orange juice, which are mandatorily fortified in other countries, such as the United States and Canada. Increasing the intake of vitamin D-rich food, with increasing sunlight exposure, of the Saudi population has reported to elevate vitamin D levels and concurrently improve bone turnover [15]. Taking the above studies into consideration, it is high time for the population of Saudi Arabia to take adequate measures to curb this problem of vitamin D deficiency.

Another worldwide problem is increasing infertility. Benyamini et al. [16] reported that about 15% of couples suffer from infertility and amongst these, 30–40% are due to reproductive problems in males [17]. Even in young males, the sperm concentration has been found to be decreased [18]. About 20% of them have sperm concentrations lower than WHO recommendations and 40% have sperm concentrations below the optimal fertility level. Over the years, male ageing has been linked to decrease in testosterone levels [19]. Recently, vitamin D metabolism has been found to be associated with androgen [20,21], but the exact mechanism by which vitamin D deficiency influences male fertility is still unclear. Various studies are being conducted to investigate the cause-effect relationship. Studies on mice showed upregulation of 19 testis-specific genes out of 2483 after treatment with vitamin D [22].

These fertility problems are prevalent in Saudi Arabian men too, especially in those who are obese or diabetic and those suffering from metabolic syndrome. In a recent study at King Abdul Aziz Hospital, Jeddah, Saudi Arabia, 19 out of 68 men observed had sexual disorders. The morning serum testosterone level was significantly low (mean value=14.14±5.38 mmol/L; reference range=9.1–55.2 mmol/L). Interestingly, testosterone level steeply declines with increased BMI. Mosli et al. [23] have also observed a similar relationship between serum testosterone level and waist circumference. Hassan et al. [24] have observed low testosterone levels in Saudi Arabian men with type 2 diabetes; 86.7% of them had erectile dysfunction (ED) accompanied with low testosterone level (8–12 nmol/L).

Hypothesis: Although vitamin D deficiency is quite common in Saudi Arabia, its effect on male fertility has not been explored. We hypothesize that low levels of vitamin D adversely affect male fertility in Saudi Arabia. Male fertility is routinely evaluated by semen analysis, and no evidence-based treatment exists at present for impaired semen quality, which is predominantly idiopathic.

Discussion

Research on mice, rats, and wild boars showed that vitamin D-deficient animals also have low fertility rates [25–29]. Detailed investigations have revealed the problems with sperm motility and poor sperm morphology make them infertile. Research shows that Vdr-null mice having deficient vitamin D receptors exhibited a 40% decrease in sperm number and a 9-fold decrease in sperm motility [25]. Calcium replacement therapy in vitamin D-deficient male rats has been shown to improve their fertility [30]. Ding et al. [31] reported that vitamin D supplementation in diabetic rats upregulated genes related to reproductive and testosterone synthesis.

In humans, cross-sectional studies have shown lower sperm motility in vitamin D-deficient (<25 nmol/l) and -insufficient (<50 nmol/l) males in comparison to the men with sufficient vitamin D levels [32–34]. Other studies have also revealed direct associations of sperm motility and sperm morphology with 25-hydroxyvitamin D levels [32,34]. A recent study by Canguven et al. [35] showed improvement in testosterone levels, metabolic syndrome, and erectile function after vitamin D
treatment in middle-aged men (Canguven et al., 2017). Other correlative studies have been performed by Sayar et al. [36] and Isik et al. [37].

More evidence of the association of vitamin D levels and male fertility comes from the observation that vitamin D receptor (VDR) and vitamin D metabolizing enzymes are expressed in Sertoli cells, germ cells, Leydig cells, spermatozoa, and epithelial cells lining the male reproductive tract [38–42]. Further studies have shown the presence of vitamin D gene CYP24A1 at the sperm annulus, which has proved to be a predictive marker for good-quality sperm [33,38]. The CYP24A1-expressing sperm is positively associated with sperm count, concentration, motility, and morphology [33].

Vitamin D is well known for its contribution in calcium absorption in the intestine and excretion in the kidney. Deficiency of vitamin D causes hypocalcemia, which directly affects the target tissues. 1a, 25-dihydroxyvitamin D3 causes a rapid increase in intracellular Ca2+ concentration in the neck of human spermatozoa, which induces sperm motility [33,42,43], improves sperm-egg binding [33], and triggers the acrosome reaction in vitro [33]. All these conditions are prerequisites for fertilization. Other studies on animal and human association further confirm this in vitro effect. Vitamin D also regulates the production of osteocalcin by the skeleton [44], whose role in fertilization is currently unclear. High vitamin D deficiency in spermatogenesis has also been reported. These exercises cause an induction in CYP17A1 expression, the key enzyme of the testosterone biosynthetic pathway [47]. Epidemiological studies on conception rate also support the positive relationship between vitamin D and fertility, as the conception rate in northern countries of the Northern Hemisphere became highest during summer [48].

Conclusions

We can conclude from the above discussion that vitamin D plays a very important role in male reproductive health of the Saudi population. There is an urgent need to mitigate the growing vitamin D deficiency conditions by increasing sunlight exposure, consumption of vitamin D-rich foods, fortified foods, or calcium and vitamin D supplementation. This would certainly improve the declining male fertility rate in Saudi Arabia.

Conflict of interest

None.

References:


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