Role of vitamin D in infertility.

Hawaldar Ranjana*

Sampurna Sodani Diagnostic Clinic, India

***Corresponding author:** Hawaldar Ranjana, Sampurna Sodani Diagnostic Clinic, India, E-mail: drranjana@sampurnadiagnostics.com

Received date: August 04, 2017; **Accepted date:** August 06, 2017; **Published date:** August 10, 2017

Citation: Ranjana H. Role of vitamin D in infertility. J Public Health Policy Plann. 2017; 1:1.

Editorial

In recent years, there has been a growing interest in studying the association of vitamin D deficiency and infertility. It has been postulated that vitamin D receptors (VDR) are found in human tissues such as male and female reproductive organs and play a major role in facilitating the biological activity of Vitamin D. Vitamin D deficiency has been advocated as a possible cause of infertility in many studies conducted in the past several years. This review article aims to systematically review the studies associating the role of Vitamin D in infertility from 2004 to 2017 and analyse their findings and limitations associated with the study.

A systematic search of scientific literature from published studies evaluating the role of vitamin D in infertility was performed in electronic databases from year 2004 to 2017. The articles included both prospective and retrospective studies available on the net.

Many researchers have studied the role of vitamin D and its association with reproductive health extensively in the last few years but there is no single consensus on its influence in reproductive health. While it is a general observation that optimal level of vitamin D is essential in PCOS, endometriosis, male infertility and IVF techniques, but there has been no significant correlation between vitamin D levels and ovulation stimulation or embryo development and Vitamin D levels. However, larger studies including all ethnic and racial groups would be required to proclaim the role of Vitamin D in infertility.

Vitamin D, also known as “sunshine hormone”, is a fat soluble hormone which plays an integral part in calcium and phosphorous homeostasis and maintainence of healthy bones and teeth and is involved in providing protection against a number of diseases such as cancer, diabetes, multiple sclerosis, cardiovascular diseases, obesity and many other diseases including its role in infertility [1-6].

Vitamin D is considered to be a prohormone and is synthesized by skin on exposure to sunlight as Vitamin D3 or cholecalciferol. Vitamin D2 or ergoclaciferol is obtained from yeast and dietary sources. Vitamin D deficiency can result from inadequate exposure to sunlight, malabsorption syndromes and certain drugs like dilantin, phenobarbitol and rifampicin which induce hepatic P450 enzymes to accelerate the catabolism of vitamin D [7].

In recent years, there has been a growing interest in studying the association of vitamin D deficiency and infertility [8-10]. It has been postulated that vitamin D receptors (VDR) are found in human tissues such as male and female reproductive organs and play a major role in facilitating the biological activity of Vitamin D [1-3] In the US, it has been estimated that about one third of the population is deficient in Vitamin D and infertility affects nearly 15.5% of the US couples and nearly 53 million people all across the globe [11,12]. Vitamin D deficiency has been advocated as a possible cause of infertility in many studies conducted in the past several years.

This review article aims to systematically review the studies associating the role of Vitamin D in infertility from 2004 to 2017 and analyse their findings and limitations associated with the study.

A systematic search of scientific literature from published studies evaluating the role of vitamin D in infertility was performed in electronic databases from years 2004 to 2017. The articles included both prospective and retrospective studies available.

The study conducted by Corbett et al. in 2004 [13] in New Hampshire USA aimed to investigate the presence of VDR in human sperm. Semen samples from 11 fertile and 20 infertile men were analysed. They concluded that VDR is present in the midpiece of human sperm and VDR expression was inversely proportional to sperm concentration in infertile men as compared to fertile controls. They observed a downward trend in VDR expression for patients with low motility irrespective of fertile status. The study was limited by small sample size [13]. In a further study conducted in 2006, they analysed semen samples from 10 fertile men and observed that VDR is expressed in mainly head/nucleus in the post acrosome portion and mid piece of sperms in all fertile men. Their study excluded all infertile men due to low or undetectable VDR expression or oligospermia, low motility and poor morphology [14]. Their study was limited by small sample size and inclusion of only fertile men.

In 2010, Anifandis et al. carried out a prospective study in Greece to measure serum and follicular fluid (FF) 25(OH) D and glucose levels in women who underwent IVF or embryo

transfer to evaluate the success rate of IVF in 101 women. (8)They observed that FF 25(OH) D had a significant correlation with embryo quality (R=0.27, P=0.027) and that FF glucose levels were lower with high Vitamin D (p-0.003). Clinically, pregnancy rates were lower with high vitamin D (P=0.047) in their study. They observed that high vitamin D and low FF glucose have a negative effect on embryo quality and IVF outcomes.

The first comprehensive analysis of the potential role of vitamin D in male reproduction was carried out by Bloomberg et al in Denmark in 2010. They analysed 13 men with orchidectomies due testicular cancer and/or prostatectomies and concluded that there was marked expression of VDR and Vitamin D metabolizing enzymes in human testis, ejaculatory tract and mature spermatozoa suggesting that Vitamin D plays a pivotal role in spermatogenesis and maturation of human sperms. [3]. However, their study was limited by the fact that they carried out their study on pathological specimens.

Ozkan et al. [5] carried out a prospective study in New York in 2010 to determine the outcome of IVF cycles in relation to Vitamin D levels in the FF of 84 infertile women. They too found a significant correlation between serum and FF vitamin D (R=0.94). They observed that women with higher Vitamin D levels were more likely to have positive outcome of IVF (P=0.013). They concluded that Vitamin D supplementation given to deficient subjects could improve fertility outcomes [5].

Ramlau et al. conducted a crosssectional study in 2011 in Denmark in 347 young men to examine the association between low serum Vitamin D and male reproductive function [15]. They observed that a high Vitamin D level was unexpectedly associated with lower crude median total sperm count and percentage of sperms with normal morphology and a high level of crude sex hormone binding globulin and FSH. Men with high level of vitamin D had 11% lower free androgen index as compared to men with adequate Vitamin D. Their study did not find any correlation between low Vitamin D levels and poor semen quality.

Bloomberg et al. in their study in 2011 analysed 300 young men for semen quality and Vitamin D levels to assess the correlation between the two. They observed a positive correlation between sperm motility and progressive motility with Vitamin D levels. ($p<0.05$) Men with lower vitamin D levels had lower proportion of motile (p=0.027), progressively motile (p-=0.035) and morphologically normal spermatozoa (p=0.004) as compared to men with high vitamin D levels. They further observed that activated Vitamin D increased intracellular calcium concentration, sperm motility and induced acrosomal reaction in mature sperms suggesting a role of vitamin D in optimal sperm function [4]. However, their study was limited by the fact that only fertile men were included in the study.

Similar findings were observed by Aleyasin et al. [1] in their prospective cohort study in 2011 in Asian men where they found a positive correlation between vitamin D levels in serum and FF (R=0.767, p=0.001). They observed that fertilization rated decreased significantly (p=0.018) and implantation rates increased (p=0.791) with higher vitamin D levels. Their observation was contrary to the observations made by other researchers. They concluded that low vitamin D has no correlation with outcome of ART [1].

In a retrospective study carried out by Li et al in California in 2012 in 1192 women of reproductive age, it was observed that majority of the infertile women had low vitamin D levels with 68.6% women having levels <32 ng/ml and 22.2% having <20 ng/ml levels. They observed that high BMI, Asian and blacks were all at high risk of vitamin D deficiency, particularly Asian women [9]. Similarly, Rainer et al in 2012 in Oklahoma retrospectively evaluated 53 PCOS women and found that vitamin D deficiency was highly prevalent in PCOS women. However, they did not find any positive correlation with levels of Vitamin D and time to pregnancy [10].

Rudick et al. in 2012 [6], in their retrospective study, aimed to validate the findings by other investigators in 188 fertile women undergoing IVF and observed that low vitamin D is associated with lower pregnancy rates in Hispanic whites (p=0.04) but not in Asians. They observed that Asians had lower pregnancy rates with low vitamin D levels (p=0.01) and that Vitamin D was lower in younger (p=0.01) and heavier (p=0.03) women and had diminished ovarian reserve (p=0.01). The reverse correlation observed in their study could be due to small sample size of Asians [6].

In 2013, Garbedian et al. [17] in Canada classified 173 women aged 18-41 years into white, black and other categories to investigate the role of Vitamin D in IVF patients. Their observation was that optimal Vitamin D levels had higher clinical outcomes of IVF (52.5%) as compared to women with low vitamin D (34.7%). However, implantation rate in both the groups was not statistically significant (p=0.6) [17].

In a prospective cross-sectional study in Italy by Paffoni et al. in 2014 to investigate IVF outcomes and Vitamin D levels in 154 Caucasian women, clinical pregnancy were 20% in women with vitamin D<20 ng/ml and 31% in women with vitamin D> 20 ng/ml (p=0.02) [18].

Rudick et al. [16] in 2014 found that Vitamin D deficient Caucasian females had lower clinical pregnancy rates as compared to Vitamin D adequate recipients (37% vs. 78%). They found that live birth rate was 31%among Vitamin D deficient subjects as compared to 59% among Vitamin D sufficient subjects. They concluded that vitamin D may be mediated through the endometrium [16]. However, Firouzabadi et al. [2] in 2014 did not find any significant correlation between pregnancy rate and serum Vitamin D levels (p=0.094) or the FF vitamin D level (p=0.170). The serum Vitamin D and FF vitamin D levels correlated significantly (p=0.000) in their study [2].

Abbasihormozi et al. [19] in 2017 published a study about the association of Vitamin D status with semen quality and reproductive hormones in Iranian sub fertile men. They observed that in normospermic men, serum vitamin D levels did not correlate with semen parameters and reproductive hormones, whereas there was a positive correlation with

vitamin D in oligoasthenotetrazoospermic men (r=0.131, p=0.028) [19].

The role of vitamin D and its association with reproductive health has been studied extensively by many researchers in the last few years but strill there is no single consensus on its influence in reproductive health. While it is a general observation that optimal level of vitamin D is essential fin PCOS, endometriosis, male infertility and IVF techniques, but there has been no significant correlation between vitamin D levels and ovulation stimulation or embryo development and Vitamin D levels. However, larger studies including all ethnic and racial groups would be required to proclaim he role of Vitamin D in infertility.

References

1. Aleyasin A, Hosseini MA, Mahdavi A, et al. Predictive value of the level of vitamin D in follicular fluid on the outcome of assisted reproductive technology. Eur J Obstet Gynecol Reprod Biol. 2011;159:132-7.
2. Firouzabadi R, Rahmani E, Rahsepar M, et al. Value of follicular fluid vitamin D in predicting the pregnancy rate in an IVF program. Arch Gynecol Obstet. 2014;289:201-6.
3. Jensen MB, Nielsen JE, Jørgensen A, et al. Vitamin D receptor and vitamin D metabolizing enzymes are expressed in the human male reproductive tract. Hum Reprod. 2010;25:1303-11.
4. Jensen MB, Bjerrum PJ, Jessen TE, et al. Vitamin D is positively associated with sperm motility and increases intracellular calcium in human spermatozoa. Hum Reprod. 2011;26:1307-17.
5. Ozkan S, Jindal S, Greenseid K, et al. Replete vitamin D stores predict reproductive success following *in vitro* fertilization. Fertil Steril. 2010;94:1314-9.
6. Rudick B, Ingles S, Chung K, et al. Characterizing the influence of vitamin D levels on IVF outcomes. Hum Reprod. 2012;27:3321-7.
7. Tangpricha V. Vitamin D deficiency and related disorders: Medscape.
8. Anifandis GM, Dafopoulos K, Messini CI, et al. Prognostic value of follicular fluid 25-OH vitamin D and glucose levels in the IVF outcome. Reprod Biol Endocrinol. 2010;8:91-5.
9. Li L, Schriock, E, Dougall K, et al. Conference abstracts. Fertility Weekly. 2012;12:17.
10. Rainer D, Davis E, Peck J, et al. Conference abstracts. Fertility Weekly. 2012:13-17.
11. Stanford JB. What is the true prevalence of infertility? Fertil Steril. 2013;99:1201-2.
12. Dabrowski FA, Grzechocinska B, Wielgos M. The role of vitamin D in reproductive health: A Trojan horse or the golden fleece? Nutrients. 2015;7:4139-53.
13. Corbett ST, Stern JE, Sundaram S, et al. Vitamin D: Is there a role in male infertility? Fertil Steril. 2004;82:S41-4.
14. Corbett ST, Hill O, Nangia AK. Vitamin D receptor found in human sperm. Urology. 2006;68:1345-54.
15. Ramlau-Hansen C, Moeller UK, Bonde JP, et al. Are serum levels of vitamin D associated with semen quality? Results from a cross-sectional study in young healthy men. Fertil Steril. 2011;95:1000-4.
16. Rudick BJ, Ingles SA, Chung K, et al. Influence of vitamin D levels on *in vitro* fertilization outcomes in donor-recipient cycles. Fertil Steril. 2014;101:447-52.
17. Garbedian K, Boggild M, Moody J, et al. Effect of vitamin D status on clinical pregnancy rates following in vitro fertilization. CMAJ Open. 2013;1:e77-82.
18. Paffoni A, Ferrari S, Viganò P, et al. Vitamin D deficiency and infertility: Insights from *in vitro* fertilization cycles. J Clin Endocrinol Metab. 2014;99:e2372-6.
19. Abbasihormozi SH, Kouhkan AR. Alizadeh association of vitamin D status with semen quality and reproductive hormones in Iranian sub fertile men. Andrology. 2017;113:118.