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Association between Vitamin D Deficiency and Occurrence of Miscarriage among Women

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Abstract:Background: *Vitamin D deficiency is a common problem in reproductive-aged women especially in the Arab nation. The association of vitamin D deficiency and miscarriage is still unclear.*
The aims *of this study were to identify risk factors for vitamin D deficiency and to examine the association of vitamin D deficiency and occurrence of miscarriage.*
Design*: A descriptive correlational research design was adopted.*
Setting*: The study was conducted at the obstetrics and gynecology clinic at Shaqra general hospital, Saudi Arabia.*
Subjects*: A total of 200 women in the child bearing age and diagnosed with abortion were recruited.*
Tools*: Two tools were used; Structured interview questionnairewhich included: socio-demographic characteristics as well as obstetric history; and Vitamin D risk factors assessment questionnaire.*
Results*: the mean age of the study sample was 37±5.37 years old. Sixty one percent of the sample had more than two abortions and 77% had abortion in first trimester. The reported non-modifiable risk factors for vitamin D deficiency were; dark skin (55%), and genetic mutation (47%). While, the modifiable risk factors were inadequate sun exposure (74%), malabsorption syndrome (20%), obesity (38.5%), low vitamin D diet (59.5%), and low socioeconomic status (14.5%). Fifty nine had insufficient vitamin D in the blood. There was a relationship between occurrence of recurrent abortion and vitamin D deficiency (p< 0,000) especially during first trimester.*
In conclusion: *There was association between Vitamin D level and first-trimester miscarriage, indicating that vitamin D concentrations in the first trimester were associated with increased risk for a subsequent miscarriage.*
Recommendation: *Modification of Vitamin D status among women may substantially reduce the frequency of miscarriage. Preconception intervention programs to focus on raising vitamin D levels in these women should be carried out in order to prevent vitamin D deficiency-linked miscarriage.*
Key Words: *Vitamin D deficiency, miscarriage, women.*

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I. Introduction

Reproductive health is an important issue worldwide, particularly in women of childbearing age [1]. One of issue, which happens during pregnancy and affects the reproductive health, is miscarriage. It is referring to the phenomenon by the loss of an embryo or fetus before the 20th week of pregnancy. The medical term for miscarriage is spontaneous abortion. It can be divided into early abortion <12 weeks) and late abortion (≥12 weeks and <28 weeks) [2]. Numerous mechanisms have been described for the pathogenesis of miscarriage, including chromosomal anomalies, uterine abnormalities, hormonal problems, infections, autoimmune disorders and thrombophilia, and up to 50% of cases have not a clearly defined etiology [3]. In Saudi Arabia, about 44% of Saudi women with high-risk pregnancy were aged between 30 and 35 years of age. Approximately 35% of them had two or more previous abortion [4].

As miscarriages are considered irreversible, prevention is probably the only way to intervene in this problem, which has detrimental psychological consequences for the woman and her partner and delays successful childbearing. Several modifiable and non-modified risk factors during pregnancy have been examined [5]. Miscarriage can happen due to smoking, alcohol drinking, uncontrolled diabetes [6], hypertension, obesity, genetic factor, cervical incompetence, low progesterone level, and environmental and

lifestyle factor [7]. Moreover, Khalifaand El-Sayed [8], reported that modifiable risks were work that requires constant motions and hard effort (37.0%), and pregnant women working more than 40h/week (28.4%). Lifestyle risk factors included drinking more than 200mg caffeine/day (87.9%), eating too much spice (39.6%), eating dates daily (37.3%), drinking cola constantly (37.0%), passive smoking (35.8%), and obesity (32.3%). Moreover, there were some obstetric risk factors for miscarriage as spacing between pregnancies, hormonal imbalance, ovarian cyst, and genital infections[5].

One of the modified risk factor of occurrence miscarriage is Vitamin D deficiency. Recent literature has demonstrated that vitamin D level was much less than the amount required maintaining health. Despite frequent exposure to ultraviolet radiation in tropical countries, some studies have shown vitamin D deficiency in these areas [9]. Vitamin D, a steroid hormone, has well-established classic function in maintaining calcium homeostasis and promoting bone mineralization [10]. In addition, vitamin D has significant roles in regulating cell proliferation and differentiation and modulating innate and adaptive immune responses [11]. Vitamin D status during pregnancy has been drawing great attention. There is some evidence suggesting that vitamin D modulates human reproductive processes [12]. Poor vitamin D status during pregnancy has been associated with preeclampsia, gestational diabetes [13], bacterial vaginosis [14], and compromised intrauterine growth [15]. According to some studies, vitamin D deficiency during pregnancy is associated with an increasing risk of preterm birth. Wagner et al. [16], reported that pregnant women with serum concentrations of vitamin D less than 20 ng/mL had 3.81 times the odds of a preterm birth compared to those with serum concentrations of vitamin D greater than 40 ng/mL.

However, the relationship of vitamin D deficiency and insufficiency in the first-trimester pregnancy with miscarriage or non-gravid childbearing aged women with spontaneous pregnancy loss history is less clear. In addition, the vitamin D metabolic pathway involves multiple enzymatic reactions. Also, vitamin D synthesis in human placenta and decidua implicate the importance of this hormone in reproductive function and is so as a risk factor of pregnancy loss [17].

To date, little is known regarding the possible associations between the levels of the enzymes been explored in relation to miscarriage in the first-trimester pregnancy. To determine whether altered vitamin D metabolic system is present in women with pregnancy loss, a study done by Hou and his college[18], measured vitamin D in pregnant women with pregnancy loss in the first trimester and non-gravid women displaying failed clinical pregnancy history in the first trimester. The objective of this study was to elucidate the association between maternal serum levels of vitamin D in the first-trimester pregnancy with the risk of pregnancy loss in a population of Chinese women. In the same time, serum calcium, phosphorus and parathyroid hormone (PTH) concentrations were measured. The study revealed that there was a strong association between low vitamin D levels and miscarriage (odds ratio 1.71; 95% confidence interval: 1.2–2.4, $P<0.001$). The regression analyses showed that PL was significantly inversely correlated with vitamin D ($P<0.01$).

II. Significant of the Study

Vitamin D deficiency and insufficiency have been considered as a common and thorny public health problem around the world, especially for pregnant women [21&22]. In Saudi Arabia, hypovitaminosis D can be considered a major public health problem with a significantly high prevalence especially among women, ranging from to ~80 to 100 % in different studies [23, 24&25]. It is associated with a variety of adverse maternal and fetal outcomes, ranging from preeclampsia, gestational diabetes, preterm delivery, intrauterine growth restriction, spontaneous abortion, and cesarean section [26&27]. However, other studies have demonstrated no association between vitamin D status and adverse pregnancy outcomes [28]. A randomized control trials and observational studies measure vitamin D late in the pregnancy, when prenatal vitamins containing 400 IU of vitamin D have been prescribed. Therefore, it sought to determine if vitamin D deficiency in the first trimester of nulliparous women is associated with clinical outcomes most associated with significant maternal and fetal morbidity and mortality [14]. In addition, a randomized control trail by Sablok et al., [29], in India showed that women who were given vitamin D supplementation during pregnancy had a 61% lower risk of preterm labor and a 47% lower risk of hypertensive complications as compared to women who were not taken supplementation. Therefore, the present study will contribute to a greater understanding to identify risk factors of vitamin D deficiency during pregnancy; and examine the association of Vitamin D deficiency and occurrence of miscarriage.

Aims of the Study:

1- To identify risk factors of vitamin D deficiency during pregnancy.
2- To examine the association of Vitamin D deficiency and occurrence of miscarriage.

Research Questions:
Q1- What are the risk factors for vitamin D deficiency during pregnancy?
Q2- Is there an association between Vitamin D deficiency and occurrence of miscarriage?

III. Subjects and Methods

Research Design:
A descriptive correlational research design was adopted to achieve the stated aims. Descriptive designs are useful to gain additional information about characteristics within a particular area of study [30]. A correlational study determines whether or not two variables are correlated. This means to study whether an increase or decrease in one variable corresponds to an increase or decrease in the other variable [31].

Setting:
The study was conducted at the obstetrics and gynecology outpatient clinic at Shaqra general hospital, Kingdom of Saudi Arabia. This clinic provides free services such as antenatal care; gynecological care and infertility treatment as well.

Sampling:
A purposive sample of 200 women in the child bearing age and diagnosed with abortion were recruited according the following criteria:

Inclusion criteria:
- Healthy women with gestational age 20 weeks or below.
- History of abortion.
- Not take vitamin D during pregnancy.

Exclusion criteria:
- Pregnant women with Type1 Diabetes Mellitus.
- Chronic kidney disease, autoimmune disease.
- Take vitamin D during pregnancy.

Sample size:
A total of (200) participants were selected according to the following statistical formula n = Z2p (1-p) /d2, where z = level of confidence according to the standard normal distribution (for a level of confidence of 95%, z = 1.96). p = estimated proportion of the population that presents the characteristic (when unknown we use p = 0.5), d = (d is considered 0.05).

Tools for data collection:
To collect data pertinent to the study, two tools were constructed and used by the researchers after reviewing related literature.

Tool 1: Structured interview questionnaire (It included 13 questions)
It entails two main sections: section one included data related to sociodemographic characteristics such as; maternal age, and type of occupation, hours of work, level of education……..ect; Section two included data related to medical history as well as, obstetrics history (gestational age; parity; gravidity; type of abortion).

Tool 2: Vitamin D risk factors assessment questionnaire (it contains 12 questions)
It was a questionnaire-based interview used to elicit details of modifiable and non-modifiable risk factor of vitamin D deficiency as dietary risk factors (low vitamin D diet); obesity; mal-absorption syndrome; genetic factors; medical factors; and other factors as; consumption of milk product, exposure to sun light; socioeconomic status. Inaddition to measuring vitamin D level in the blood.

Content validity and reliability:
The tools were developed by the researchers after extensive literature review and tested for content validity by a jury of five experts in obstetric and maternity nursing to reach consensus of the best form to be implemented. Modifications were carried out according to the panel judgment on clarity of sentences and appropriateness of the content. Test reliability of the proposed tools was tested by (cronbach's alpha=0.84), showed a strong significant positive correlation between the items of tools. Also, tools were assessed by applying the questionnaire on 10 women using test–retest reliability.

Pilot study:

A total of 10% of the sample were included in the pilot study in order to assess the feasibility and clarity of the tools and determine the needed time to answer the questions. The pilot study lasted for two weeks. Based on its result minimal changes were carried out. Pilot study revealed that; the average length of time needed to complete the structured interview was approximately 15 minutes with each woman. Sample included in the pilot study were excluded from the study.

Ethical considerations:

An official permission was taken from the authoritative personnel in the general hospital. The researchers introduced themselves to the women who met the inclusion criteria and they were informed about the aim of this research in order to obtain their acceptance to share in this research. Participants were informed that their participation will be on voluntary basis, and anonymity and confidentiality of the participants were maintained at all times

Procedure:

An official permission was granted from the administrative personnel of the Shaqra general hospital, Saudi Arabia, after explaining the purpose of the study. All women diagnosed with abortion were invited to participate in the current study, ensuring the confidentiality of the information, and they are free to withdraw at any time without any plenty. Data collection was carried out from the first of September, 2018 till March 2019. After obtaining approval and informed consent to conduct the study, data were collected three days/ week through interviewing questionnaire with each woman by the researchers individually using constructed questionnaire. Modifiable and non-modifiable Risk factors for vitamin D deficiency were assessed using the face-to-face interview with each woman individually by the researchers. Each women needs 25–30 min to complete the research questionnaires.

Measuring Vitamin D Level in the Blood:

A venous blood sample (5 ml) was collected at the same time for vitamin D estimation and sent to the reference laboratory of Shaqra general hospital to assess serum Vitamin D concentrations using standard routine biochemical methods. According to Holick, [32] the samples were promptly centrifuged and serum stored at -20° C until analysis. The samples were centrifuged and serum extraction was done in the field. Then, the samples were sent to laboratory for analysis and were frozen immediately. Afterwards, 25-hydroxy vitamin D (25(OH) D) level was measured using High Performance Liquid Cromatogheraphy (HPLC). Vitamin D level was classified into three categories based on Begum, Saikia Pathak, & Deka, [33].

1. Vitamin D deficient – 25(OH) D< 20 ng/ml.
2. Vitamin D insufficient – 25(OH) D – 20- <30 ng/ml.
3. Vitamin D normal – 25(OH) D- 30-100 ng/ml.

Statistical Analysis:

The collected data were scored, tabulated and analyzed using Statistical Package for the Social Science (SPSS) program version 23. Descriptive as well as parametric inferential statistics was utilized to analyze data pertinent to the study. Level of significance was set at $p < .05$. Correlate bivariate Pearson test was used to analyze data.

IV. Results

The result of the study is divided into three parts as the following:

Part one: Demographic and Obstetrical Data.

Part 2: Objective one (identify risk factors of vitamin D deficiency during pregnancy).

Part 3: objective two (examine the association of Vitamin D deficiency and occurrence of miscarriage).

Part one: Demographic and Obstetrical Data

Table1: Frequency Distribution of the Socio-demographic Characteristics of the Sample (N = 200)

Characteristics	No.	%
Age:		
20-30 years	29	14.5
31-40 years	113	56.5
> 40 years	58	29.0
Age (Mean ± SD)	37.0 ± 5.37	
Residence		
Urban	13	6.5
Rural	187	93.5
Educational Level:		
Illiterate	6	3.0
Primary	41	20.5
Secondary	66	33.0
University	87	43.5
Occupation		
Working	132	66.0
Not working	68	34.0
Socioeconomic status		
Low	29	14.5
Middle	135	67.5
High	36	18.0
BMI (kg/m2)		
Underweight		
Normal	7	3.5
Overweight	116	58.0
Obese	37	18.5
	40	20.0

Table (1) shows that, the mean age of the sample was 37.0 ± 5.37 years, 93.5% were from rural area, and less than half of them (43.5%) have university education. On the other hand, more than two-third (66%) of the women were working and were from middle socioeconomic status (67.5%).

Table 2: Frequency Distribution of Obstetrics History

Items	No.	%
Number of Pregnancies		
< 3	37	18.5
3-6	132	66.0
> 6	31	15.5
Number of previous Deliveries		
Primipara	37	18.5
Multipara	163	81.5
Antenatal care Follow up		
Yes	189	94.5
No	11	5.5
Number of abortion		
≤ 2	78	39.0
> 2	122	61.0
Number of children		
≤ 3	137	68.5
4-6	47	23.5
> 6	16	8.0
Gestation (current pregnancy)		
First trimester	154	77.0
Second trimester	46	23.0

The majority of the sample (81.5%) wasmulti-parous, more than two-third (77%)was in the first trimester of pregnancy, and two-third (61%) had history of two or more abortions (Table, 2).

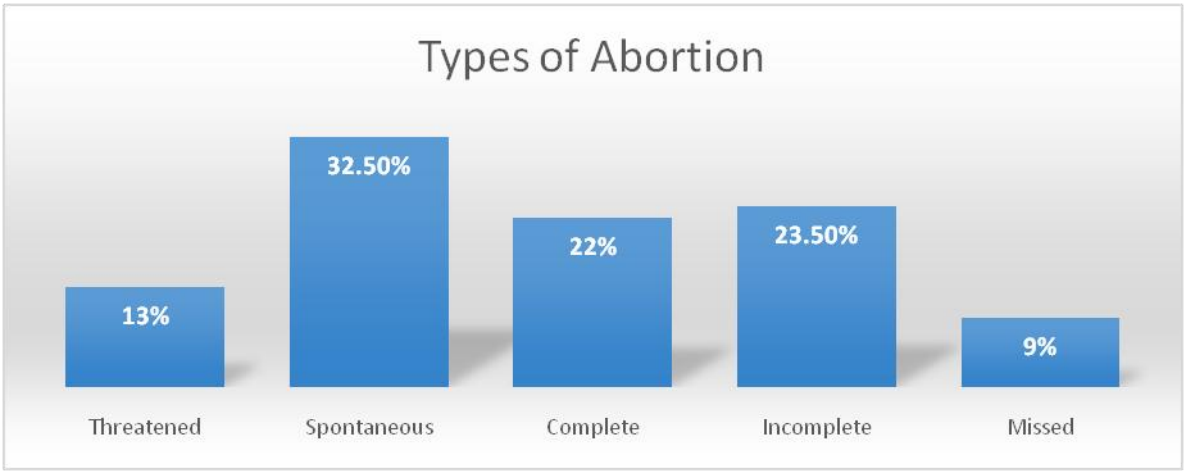

Fig. (1) Distributions of Types of Abortion among the Sample

Figure (1) showed that 32.5%of the women had spontaneous abortion, while, 23.5% had incomplete abortion. On the other hand, a few cases (13%) had threatened abortion and 9% had missed abortion

Table 3: Frequency Distribution of the Risk factors for Vitamin D Deficiency (N = 200)

Items	No.	%
Non-Modifiable Risk Factors		
- Dark skin pigmentation	110	55.0
- Genetic mutation	95	47.5
- Age **(Mean ± SD)**	37.0 ± 5.37	
- Medication use	44	22.0
- Hyperthyroidism	16	8.0
- Hypertension	15	7.5
- Hyperglycemia	22	11.0
- Mal-absorption syndrome	40	20.0
Modifiable Risk Factors		
- Inadequate sun exposure	149	74.5
- Obesity	77	38.5
- Low vitamin D diet	119	59.5
- Low Socioeconomic status	29	14.5
- Medication use	44	22.0

Table (3)shows the non-modifiable and modifiable risk factors for vitamin D deficiency among the studied sample. In Relation to the non-modifiable risk factors, it was found that almost half (55%) of the studied sample had Dark skin pigmentation and Genetic mutation (47.5%). Regarding to the modifiable risk factors, it was found that a variety of risk factors affect the vitamin D level in the blood, such as inadequate sun exposure (74.5%), Low vitamin D diet (59.5%), and the obesity (38.5%).

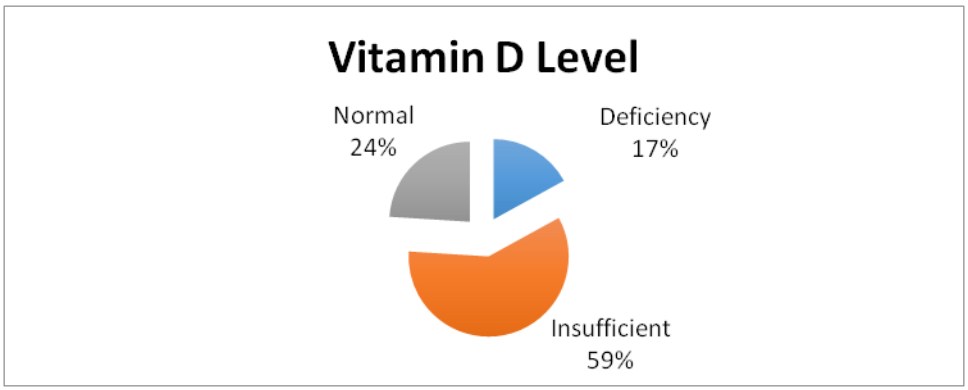

Fig. (2). Distributions of Vitamin D Level in the Blood among the Studied Sample.

Figure (2): this figure represented that more than half of the studied women (59%) had insufficient vitamin D level in the blood, while less than one-third (24%) had normal levels.

Table 4: Relationship between Number of Abortions and Vitamin D Level in Blood

Number of abortions	Vitamin D level in blood			χ^2	*P-value*
	Normal N= 42	**Insufficient N= 73**	**Deficiency N= 85**		
≤ 2 (n= 78)	30	15	33	28.97	0.000**
> 2 (n= 122) (Recurrent abortion)	12	58	52		

**** Highly Statistically Significant Differences at P ≤ 0.001**

Table (4)revealed that the recurrent abortion was affected by the vitamin D levels in the bloodamong the studied women, which indicated that the number of abortions was increased with insufficient and deficient levels of vitamin D in the blood with a highly statistically significant differences at ($\chi 2$ =28.97and P ≤ 0.001).

Table 5: Relationship Between types of Abortion and Vitamin D Level in the Blood

Type of abortion	Vitamin D level in Blood			χ^2	*P-value*
	Normal N= 42	**Insufficiency N= 73**	**Deficiency N= 85**		
	Freq.(%)	**Freq.(%)**	**Freq.(%)**		
Threatened (n= 26)	7 (16.7%)	10(13.7%)	9(10.6%)	2.6	0.95
Spontaneous (n= 65)	14(33.3%)	21(28.7%)	30(35.3%)		
Complete (n= 44)	8 (19.05%)	17(23.3%)	19(22.4%)		
Incomplete (n= 47)	8 (19.05%)	19(26.1%)	20(23.5%)		
Missed (n= 18)	5 (11.9%)	6(8.2%)	7(8.2%)		

Table (5)revealed that there were no statistically significant differences between the types of abortion and the Vitamin D Levels in blood among the studied women. The majority of the sample, who had insufficient or deficient vitamin D levels, had spontaneous, incomplete and complete abortion respectively.

Table 6: Relationship between Pregnancy Trimesters and Vitamin D Level in the Blood

Trimesters	Vitamin D level in blood			χ^2	*P-value*
	Normal N= 42	**Insufficiency N= 73**	**Deficiency N= 85**		
	Freq.(%)	**Freq.(%)**	**Freq.(%)**		
First trimester (n=154)	35(83.4%)	49(76.1%)	70(82.4%)	6.799	0.05*
Second trimester (n=46)	7(16.6%)	24(32.9%)	15(17.6%)		

*** Statistically Significant Differences at P ≤ 0.05**

Table (6): This table indicated that most of women had insufficient or deficient vitamin D levels in the bloodmore in first trimesterthan second trimester with statistically significant differences at (χ^2 =6.799 and P ≤ 0.05).

V. Discussion

Many of researches have been published to study the effect of vitamin D in human illness. A limited number of publications studied vitamin D deficiency in relation to diseases beyond bone health [34]. The current descriptive correlation study was conducted to examine the risk factors for vitamin D deficiency and the association of vitamin D deficiency and occurrence of miscarriage. The mean age of the sample was 37.0±5.37 years; most of them were from rural area and were working. More than two third were from middle socioeconomic status and had more than three pregnancy and almost three quarter were in first trimester. Moreover, more than one third had spontaneous abortion.

Vitamin D deficiency has risk factors which are non-modifiable and modifiable. Regarding the non-modifiable risk factors, the current study revealed that, more than half of the sample had dark skin, and almost half had genetic mutation. This finding is matched with Chawla, etal., [35]. who reported that Black women had much lower vitamin D concentrations as compared to White women. In relation to modifiable risk factors, about three quarter of the sample didn't expose to sun. Vitamin D concentration has been linked to sun exposure and sunshine are inhibited by skin pigmentation and consequently affects reproductive health [36&37]. Also, all the women are covered with their dress which inhibits exposure to sun. Vitamin D deficiency has also been linked to higher rates of first trimestermiscarriage [38], suggesting that sun exposure during and soon after conception may affect the number of conceptions that survive until birth [39&40].

Regarding diet type as a modifiable risk factor, the current research had shown that, about two third had low vitamin D diet. Diet is known to affect female fertility [41]. Vitamin D is an important contributor to regulate the synthesis of several hormones including oestradiol, progesterone and human chorionic gonadotrophin. These hormones are all essential in maintaining the regulation of utero-placental blood flow and maternal immune-tolerance to the embryonic allograft [42]. Humans produce vitamin D by exposure to sunlight or from or dietary supplements. Vitamin D is found naturally in only very few foods such as fatty fish, fish liver oils, and eggs. [43]. Socioeconomic status is considered one of the modifiable risk factors. Only few cases (more than one tenth) of the sample had low socioeconomic status. However, Al-Agha, etal., [44], stated that the mean vitamin D level was higher in low-income families than those with average and high incomes.

The association between vitamin D deficiency and various adverse pregnancy outcomes has been investigated in recent years, however, till now, no randomized controlled trial has been done to investigate the effect of vitamin D concentrations on the occurrence of miscarriage as a primary outcomes ([38]. The second objective of the current study was to examine the association of vitamin D deficiency and occurrence of miscarriage. About two third had insufficient Vitamin D level (25(OH) D – 20- <30 ng/ml), and near one quarter had normal level (25(OH) D- 30-100 ng/ml). These findings may be related to the factors affecting Vitamin D level as inadequate exposure to sun, inadequate diet containing vitamin D, and climate temperature. This finding is in the same line with Al-Mogbel [24] who investigated vitamin D levels in Saudi females in the childbearing period and reported that all participants had hypovitaminosis D. Despite abundant sunlight, hypovitaminosis D is highly prevalent among the Saudi people. It is more frequent in the young and middle-aged group of apparently healthy Saudi adults and in females more than males [34].

There were highly statistically significant differences between occurrence of recurrent abortion and the Vitamin D Levels in Blood among the studied sample, as almost half of the sample who had recurrent abortion had insufficient vitamin D level. In a small Danish cohort study, 3 women with miscarriage between 10 and 22 wks of gestation had lower 25(OH)D than 84 controls who completed their pregnancy [45]. In addition, in an Australian cohort, no significant difference was found between 25(OH)D concentrations in gestational weeks 10–14 in 3714 women with no adverse outcome of pregnancy vs. 39 women who miscarried, with mean 25(OH)D concentrations of 56.9 nmol/L (95% CI: 43.9, 70.8) vs. 53.5 nmol/L (95% CI: 42.4, 61.7) [43].

The study found that 25(OH)D was related to miscarriage in the first trimester. This result may be attributable to different mechanisms and underlying etiologies. Also, may be due to different management strategies and can be considered distinct disease entities. Yet, the association to first-trimester miscarriages may also be due to the 25 (OH) D concentrations being more representative of the serum concentrations at the time of miscarriage. Moreover, it is possible that 25(OH) D has a protective role against miscarriage. Vitamin D has been implicated as a regulator of innate and adaptive immune functions [13]. Accordingly, vitamin D concentrations in human placenta may have a direct impact on the cytokine profile and the inflammatory response [46]. In a recent study of 133 women with 3 or more recurrent pregnancy losses, women with 25(OH)D “30 ng/mL (75 nmol/L) had increased risk of autoimmune and abnormal cellular immune responses [47]. Similarly, in vitro studies involving endometrial cells from women with spontaneous recurrent miscarriage demonstrated that stimulation with 1,25(OH)2-D3 modulated the release of cytokines [17]. It has also been suggested that vitamin D has an active role at the feto-maternal immunologic interface and hence a role in miscarriage. Vitamin D insufficiency suggesting that hypovitaminosis D may be has an important preventable risk factor for miscarriage in the first trimester.

VI. Conclusion

In conclusion, focusing on association between Vitamin D level and first-trimester miscarriage, the results of the present study indicated that, vitamin D concentrations in the first trimester were associated with increased risk for a subsequent first-trimester miscarriage. These findings suggest a protective role for vitamin D against miscarriage. The non-modifiable risk factors for vitamin D deficiency were; dark skin (55%), and genetic mutation (47%). While the modifiable risk factorswere; inadequate sun exposure (74%), obesity (38.5%), low vitamin D diet (59.5%), low socioeconomic status (14.5%), medication use (22%), hyperthyroidism (8%), hypertension (7.5%), and hyperglycemia (11%).

Recommendations: Based on the finding of this study:

For Practice:

- Routine request of 25-hydroxy vitamin D test and prescription of vitamin D supplements are important in women before conception.
- Increase local availability of vitamin D supplements for at-risk groups.

- Raise awareness ofthe health care providers, social care and other relevant practitioners of the importance of vitamin D.
- Develop national activities to increase awareness about vitamin D among women in child-bearing period.
- Modify the risk factors for vitamin D deficiency as adequate exposure to sun.

For Research

- Replicate the study with larger sample size generalization.
- Randomized controlled trials should be performed to investigate the possible effect of increasing 25(OH)D concentrations by supplementation in early pregnancy or even preconception.

For Public

1) Raise awareness of the importance of vitamin D supplements and its benefitsamong the pregnant women.
2) Adequate exposure to sunlight.
3) Balanced diet provides all the nutrients needed except vitamin D, as few foods naturally contain it. Only oily fish is a significant source, while egg yolks, meat and a few fortified foods provide small amounts.
4) Monitor and evaluate the provision and uptake of vitamin D supplements.

Conflict of Interest

Authors declare no conflict of interest.

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References

[1]. C. Park, , M. Y., Kang , D., Kim, J., Park, H., Eom, &E. A. Kim. Prevalence of abortion and adverse pregnancy outcomes among working women in Korea: A cross-sectional study. PloS one, (2017). 12(8), e0182341.
[2]. X., Hu, M., Miao, Y., Bai, N., Cheng, &X. Ren. Reproductive Factors and Risk of Spontaneous Abortion in the Jinchang Cohort. International journal of environmental research and public health, (2018). 15(11), 2444.
[3]. The Practice Committee of the American Society for Reproductive Medicine. Evaluation and treatment of recurrent pregnancy loss: a committee opinion. Fertil Steril 2012; 98: 1103–1111. [PubMed] [Google Scholar]
[4]. [4]. SK, Hafez LS, Dorgham & SAM Sayed. Profile of high risk pregnancy among Saudi women in Taif-KSA. World J Med Sci (2014). 11:90–97.
[5]. SF Nilsson, PK, Andersen, K Strandberg-Larsen, AM Andersen. Risk factors for miscarriage from a prevention perspective: a nationwide follow-up study. BJOG 2014. 121:1375–1385
[6]. G., Costello. What is miscarriage?. 2013Available at: http://www.mergerwatch.org/…/pdf. [Accessed 20 August 2013].
[7]. CH., Rodriguez. 5 steps to decreasing the chance of recurrent miscarriages2014. Available at: http://natural-fertility-info.com/preventing-miscarriage. [Accessed 20 September 2015].
[8]. E.T.M., Khalifa, TE El-Sayed Amr. The modifiable and nonmodifiable risk factors for miscarriage. Egypt Nurs J 2016;13:169-77
[9]. SF Nilsson, PK, Andersen, K Strandberg-Larsen, AM Andersen. Risk factors for miscarriage from a prevention perspective: a nationwide follow-up study. BJOG 2014. 121:1375–1385
[10]. M Norval, HC Wulf. Does chronic sunscreen use reduce vitamin D production to insufficient levels? Br. J. Dermatol. 2009,161(4):732- 736.
[11]. O., Kuniaki, D., Svetlana, H., Ae-Ra, B., Kenneth, et al. Vitamin D deficiency may be a risk factor for recurrent pregnancy losses by increasing cellular immunity and autoimmunity. Human Reproduction 2013,. 0(0): 1-12.
[12]. DD., Bikle, J, Adams, & S. Christakos. Vitamin D: production, metabolism and clinical requirements//Rosen C. Primer on Metabolic Bone Diseases. Hoboken: John Wiley and Sons, 2013: 235–245.
[13]. V., Lagishetty, NQ,Liu,& M.Hewison. Vitamin D metabolism and innate immunity. Mol Cell Endocrinol 2011;347:97–105. Google Scholar Crossref PubMed.
[14]. E.,Lerchbaum, & T., Rabe. Vitamin D and female fertility. Current Opinion, Obstetric and Gynecology. 2014; 26: 145–150.[PubMed]
[15]. GJ., Cho, SC., Hong, MJ., Oh, HJ., & Kim. Vitamin D deficiency in gestational diabetes mellitus and the role of the placenta. Am J ObstetGynecol 2013; 209: e1–e8. [PubMed]
[16]. LM., Bodnar, MA, Krohn, & NH.,Simhan. Maternal vitamin D deficiency is associated with bacterial vaginosis in the first trimester of pregnancy. J Nutr 2009; 139: 1157–1161. [PMC free article][PubMed]
[17]. ER., Leffelaar, TG, Vrijkotte, & M. van Eijsden. Maternal early pregnancy vitamin Dstatus in relation to fetal and neonatal growth: results of the multiethnic Amsterdam Born Children and their Development cohort. Br J Nutr 2010; 104: 108–117. [PubMed]
[18]. C.L Wagner, C., Baggerly, S.L. McDonnell, L., Baggerly, S.A., Hamilton, J. Winkler, et al. Post-hoc comparison of vitamin D status at three time points during pregnancy demonstrates lower risk of preterm birth with higher vitamin D closer to delivery. J. Steroid Biochem. Mol. Biol. 2015, 148, 256–260. [CrossRef] [PubMed].
[19]. M., Tavakoli, M., Jeddi-Tehrani,A., Salek-Moghaddam, S., Rajaei, A Mohammadzadeh, S Sheikhhasani, GE Kazemi-Sefat, AH Zarnani. Effects of 1,25(OH)2 vitamin D3 on cytokine production by endometrial cells of women with recurrent spontaneous abortion. Fertil Steril 2011;;96:751-7.
[20]. W., Hou , XT., Yan , CM., Bai, XW., Zhang , LY., Hui , XW., Yu. Decreased serum vitamin D levels in early spontaneous pregnancy loss. European Journal of Clinical Nutrition (2016) 70, 1004–1008; doi:10.1038/ejcn.2016.83; published online 25 May 2016

[21]. , K. T Kanatani., T., Nakayama, Y., Adachi, K.,Hamazaki, K., Onishi, Y., Konishi, &, H Inadera. High frequency of vitamin D deficiency in current pregnant Japanese women associated with UV avoidance and hypo-vitamin D diet. PloS one, 2019, 14(3), e0213264

[22]. C. A., Baggerly, R. E., Cuomo, C. B., French, C. F., Garland, E. D., Gorham, W. B., Grant, & M. Pittaway. Sunlight and vitamin D: necessary for public health. Journal of the American College of Nutrition,2015, 34(4), 359-365.

[23]. Al GK.,-Shaikh, GH., Ibrahim, AA., Fayed, H., Al-Mandeel . Impact of vitamin D deficiency on maternal and birth outcomes in the Saudi population: a cross-sectional study. BMC Pregnancy and Childbirth, 2019, Volume 16, Number 1, Page 1

[24]. ES. Al-Mogbel, Vitamin D, status among Adult Saudi Females visiting Primary Health Care Clinics. Int J Health Sci (Qassim) 2012;6:116–126. doi: 10.12816/0005987. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[25]. AM Siddiqui, HZ. Kamfar. Prevalence of vitamin D deficiency rickets in adolescent school girls in Western region, Saudi Arabia. Saudi Med J. 2007;28:441–444. [PubMed] [Google Scholar]

[26]. Y. H., Chen, L., Fu, J. H., Hao, Yu, , P., Zhu, H., Wang, &D. X. Xu,. Maternal vitamin D deficiency during pregnancy elevates the risks of small for gestational Z., age and low birth weight infants in Chinese population. The Journal of Clinical Endocrinology & Metabolism, 2015, 100(5), 1912-1919.

[27]. L. L., Qin, F. G., Lu, S. H., Yang, H. L., Xu, &B. A. Luo. Does maternal vitamin D deficiency increase the risk of preterm birth: a meta-analysis of observational studies. Nutrients, 2016, 8(5), 301.

[28]. C. E., Powe, E. W., Seely, S., Rana, I., Bhan, J., Ecker, S. A., Karumanchi, & R. Thadhani. First trimester vitamin D, vitamin D binding protein, and subsequent preeclampsia. Hypertension, 2010, 56(4), 758-763.

[29]. A., Sablok, A., Batra, K., Thariani, A., Batra, R., Bharti, A. R., Aggarwal, & H. Chellani. Supplementation of vitamin D in pregnancy and its correlation with feto-maternal outcome. Clinical endocrinology, 2015, 83(4), 536-541.

[30]. N, Burns & S. Grove The practice of nursing research: Conduct, critique, and utilization (5th ed.). St. Louis, MO: Elsevier; 2005. 232-233. PMid:15787860

[31]. DF, Polit,& CT. Beck Essentials of nursing research: Appraising evidence for nursing practice (7thed.). Lippincott Williams and Wilkins.2009. 189.

[32]. M.F. Holick. Vitamin D status: measurement, interpretation, and clinical application. Annals of epidemiology, 2009. 19(2), 73-78.

[33]. F., Begum., M., Saikia Pathak, G. Deka,.Effect of Vitamin D Deficiency on the Outcome of Pregnancy . Scholars Journal of Applied Medical Sciences (SJAMS). Sch. J. App. Med. Sci., 2017; 5(7A):2513-2519.

[34]. NM, Al-Daghri, OS, Al-Attas,MS, Alokail,KM, Alkharfy,SM, Yakout, NJ, Aljohaniet al. Lower vitamin D status is more common among Saudi adultswith diabetes mellitus type 1 than in non-diabetics. BMC Public Health.2014;14:153.

[35]. Chawla D, Fuemmeler B, Benjamin-Neelon SE, Hoyo C, Murphy S, Daniels JL (2019). Early prenatal vitamin D concentrations and social-emotional development in infants, The Journal of Maternal-Fetal & Neonatal Medicine, 32:9, 1441-1448, DOI: 10.1080/14767058.2017.1408065

[36]. L.M. Bodnar, H.N. SimhanVitamin D may be a link to black-white disparities in adverse birth outcomes Obstet. Gynecol. Surv. (2010), 10.1097/OGX.0b013e3181dbc55b

[37]. D. Borradale Investigating the Association between Sun Exposure and Folate Degradation in the Human Body PhD dissertation School of Public Health and the Institute of Health and Biomedical Innovation, Queensland University of Technology (2013) Google Scholar

[38]. L.B. Andersen, J.S. Jørgensen, T.K. Jensen, C. Dalgård, T. Barington, J.Nielsen, S.S. Beck,Nielsen, S., etal.,. Vitamin D insufficiency is associated with increased risk of first trimester miscarriage in the Odense Child Cohort The American journal of clinical nutrition, 102(3), 633-638.

[39]. D. Slusky, R.J. ZeckhauserSunlight and protection against influenza SSRN (2018), 10.2139/ssrn.3135479Google Scholar

[40]. Trivers and Willard, 1973

[41]. A., Hossein-nezhad & M.F. Holick. Vitamin D for health: A global perspective. Mayo. Clin. Proc. 2013;88:720–755. doi: 10.1016/j.mayocp.2013.05.011. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[42]. R., Sharma, K.R., Biedenharn, J.M., Fedor, A., Agarwal. Lifestyle factors and reproductive health: taking control of your fertility. Reprod Biol Endocrinol. 2013 Jul 16;11:66. doi: 10.1186/1477-7827-11-66.

[43]. A., Mousa, S., Abell, , R., Scragg, B., De Courten. Vitamin d in reproductive health and pregnancy.Semin Reprod Med. 2016; 34: e1–13

[44]. I., Bendik, A., Friedel, F. F., Roos, , P., Weber& M.,.Eggersdorfer. Vitamin D: a critical and essential micronutrient for human health. Frontiers in physiology,2014, 5, 248. doi:10.3389/fphys.2014.00248

[45]. AE, Al-Agha,AA, Alsharief,MS, Ahmed,AY Nassir. The Effect of Socioeconomic Status on Vitamin D Level in Children's and Adolescents Living at Jeddah, Saudi Arabia. Evid Based Med Pract 2016, 2: 109. Doi: 10.4172/2471-9199.1000109

[46]. UK, Møller S, Streym L, Heuckendorff L, Mosekilde L. Rejnmark. Effects of 25OHD concentrations on chances of pregnancy and pregnancy outcomes: a cohort study in healthy Danish women. Eur J Clin Nutr 2012;66:862–8. Google Scholar Crossref PubMed

[47]. FJ,Schneuer,CL,Roberts,C,Guilbert,JM,Simpson,CS,Algert AZ, V., Khambalia, etal.,. Effects of maternal serum 25-hydroxyvitamin D concentrations in the first trimester on subsequent pregnancy outcomes in an Australian population. Am J Clin Nutr 2014;99:287–95. Google Scholar Crossref PubMed

[48]. L,Díaz,N,Noyola-Martinez,D., Barrera, G., Hernandez, E., Avila, A., Halhali, F., Larrea. Calcitriol inhibits TNF-alpha–induced inflammatory cytokines in human trophoblasts. J Reprod Immunol 2009;81:17–24. Google Scholar Crossref PubMed

Nagwa A. El Fadeel Afefy. "Association between Vitamin D Deficiency and Occurrence of Miscarriage among Women: Developing Clinical Module to Improve Pregnancy Outcomes" .IOSR Journal of Nursing and Health Science (IOSR-JNHS), vol. 8, no.03 , 2019, pp. 53-62.