

Awareness among mothers of Down syndrome children on the importance of folic acid consumption during pregnancy

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Abstract

Objective: The maternal use of folic acid supplementation particularly during the preconception period has been suggested to thwart Down syndrome, thus the awareness among the mothers of Down syndrome children regarding folic acid consumption and other factors was assessed in this study.

Methods: In this population-based case study, mothers of children with Down syndrome [n=192] living in the city of Riyadh, Kingdom of Saudi Arabia, were enrolled through schools run by The Down syndrome society. Using a specially structured questionnaire that included questions on socio-demographic variables, women's knowledge about folic acid supplementation, and timing of supplementation was evaluated.

Results: Analysis of data indicated children born to mothers who were 35 and above failed to follow recommended Folic acid supplementation. Around 70% percent of the DS mothers started taking supplementation after a confirmed pregnancy. Children were more likely to be born with DS if they were the 4th or more, child born to the same mother in the family. The rate was observed to be higher if they were born to mothers with even higher parity [>4].

Conclusion: The results of this study imply that folic acid supplementation is crucial for the prevention of Down syndrome before conception, as well as for the post-conception period in all women, especially for women who are 35 years and over and women with high parity.

Keywords: Down syndrome, Folic Acid, Pre-conception Supplementation

1.Introduction

Down Syndrome (DS) is the most common chromosomal disorder also known as trisomy 21, which results from complete or partial triplication of chromosome-21[1;2]. It is characterized by congenital heart defects, cognitive and language dysfunction along with neuromotor and sensory deficits [2].

The overall incidence of DS worldwide is 1 in 800 live births [2] with an estimate of over 210,000 people suffering from DS over the age of 55 in the US only. It has been reported that the prevalence of DS has increased by 31.1% live births from the year 1979 through 2003 [1]. The incidence within the Arabian countries has been reported to be 1.93-3.5 per 1000 live births, whereas within the Kingdom of Saudi Arabia, it is 1.8 per 1000 live births [1;3-5]. The explanation of this increase is the significantly higher proportion of prenatally diagnosed fetuses with Down syndrome and an increasing part of women over 35, but new

etiological factors cannot also be excluded as mentioned previously by Métneki and Czeizel(2005)[6].

The most common risk factor for DS is advanced maternal age but many DS children are also born to mothers younger than 35 years suggesting other factors that influence the DS etiology[7;8]. Other factors may include the presence, in at least one parent, of an extra or structurally abnormal chromosome 21 material or the birth of a previously affected offspring [9]. There is also an increase in the risk of DS with increasing parity in both younger (<35 years) and older (>35 years) women [10].

Environmental factors, such as a women's exposure to folic acid may also affect chromosome segregation during oocyte development [11]. Folic acid is an essential B-vitamin that is required for one-carbon biosynthetic and epigenetic processes [12;13]. Deficiency or lower folic acid intake has been linked to a high risk of neural tube defects and, therefore, folic acid supplementation is recommended pre- and post-

conception [14]. Many researches show polymorphisms in genes involved in the folic acid pathway which play a role in the modulation of the maternal risk for DS [14-16]. Lack of folic acid supplementation is a potential risk factor for chromosome-21 non disjunction [11].

Dietary intervention studies show that genomic instability decreases when folic acid intake is above 5mg per day [17]. In earlier times, the traditional Arabian foods used to have significant amount of folic acid and other nutrients but due to recent westernization, change in eating habits, and lack of knowledge about the importance of folic acid pre- and post-conception may have a role in the increase of Down syndrome occurrence. This study examined the awareness, knowledge and general practices of folic acid supplementation and other factors among women who have given birth to DS children in the last year.

2. Methods

2.1 Participants

Data was collected from women living in Riyadh, Kingdom of Saudi Arabia, who had given birth to a DS child within the last two years. A total of 192 participants were chosen from the Down syndrome charitable association, Riyadh, Saudi Arabia over a period of eight months and three were excluded from the study due to missing information. Approval to conduct the study was obtained from the Down syndrome association and consent was obtained from the families before administering a structured questionnaire to the study participants. Finally the study was approved by the ethical committee and the IRB of the College of Applied medical sciences. The questionnaire was administered in person by trained study personnel.

2.2 Questionnaire

The questionnaire included socio-demographics and awareness on the use of folic acid supplementation at the time of pregnancy among other factors. Folic acid awareness was assessed as ever having heard of folic acid, knowledge of its role in reducing chances of birth defects as well as knowing the best time and duration of taking folic acid. Questions regarding folic acid use by the participant's mothers and the participant's husbands and the consideration for prenatal testing were also included. A question on parity was also examined as a risk factor for DS among these women.

2.3 Data Analysis

Data analysis was completed using statistical analysis software SPSS 20. Descriptive statistics (frequency and percentages) were calculated for participants demographic and folic acid knowledge assessment.

3. Results

3.1 Characteristics of the study participants

Table 1 lists the demographics and characteristics of the study participants. About 80% (n=152) of the total 192 participants, were 35 years or above and the rest were below

35 years at the time of giving birth to a DS offspring. Fifty two percent of the women were normal weight while 26.5% and 20.8% were overweight and obese according to the BMI, respectively. The majority of the women had completed high school (41.1%) and graduation (46.3%). Only 4.1% of the women were illiterate or not educated at all while 8.3% had completed primary school. About 40.1% of the participants reported monthly household incomes of \$1500-2666 and 43.2% had incomes of \geq \$2666 while only 16.6% of the participants had income of \leq \$1500.

3.2 Knowledge of folic acid consumption during pregnancy

Table 2 summarizes the responses to questions asked in order to assess the general awareness regarding folic acid and its use. Most women (78.6%) answered in affirmative about their knowledge and importance of folic acid use and it was directly influenced by their educational status. Out of the total 192 participants, only 49 (25.5%) said they had an idea about the importance of folic acid and its role in birth defects. 82 (42.9%) of the respondents said they were not sure. About 33% had absolutely no idea about the possible role folic acid deficiency could have on birth defects.

Surprisingly, 136 women (70.8%) took folic acid when pregnant while 17 (8.8%) did not take it regularly. Among those participants who took folic acid, 123 (90.8%) started only after conception while only 13 (9.2%) took it preconceptionally. About twenty five percent of the participants took folic acid for one or 2 months after conception, while the majority (68.6%) took it for three months or more after pregnancy confirmation. Only 7.8% took it a month or more before conception.

When asked about the consumption of folic acid by the DS child's father and maternal grandmother, the majority denied taking any folic acid supplements. Of the 192 women asked about prenatal testing (e.g., amniocentesis), 97.3 percent denied having considered any intervention or testing during their pregnancy, since most were of the opinion of amniocentesis being a harmful procedure.

Since doses of folic acid and iron have been studied to have preventive effect against DS, we asked whether the participants had taken iron during their pregnancy. One hundred seventy nine women (93.2%) said they had taken iron along with folic acid supplementation. Among the women who took iron, only 3 of them (1.6%) took it before conception while 8 (4.4%) took it in the first trimester while 168 (93.85%) took it in the second trimester or later. When asked about the dietary intake of foods rich in folic acid during pregnancy, 92% agreed to having switched to healthier foods when they found out they were expecting but could not recall the foods taken specifically, so the dietary intake was not recorded.

Higher parity was seen to be associated with an increased risk of giving birth to DS babies for both women \leq 35 years or \geq 35 years but the association was stronger among older women (Figure 1). Majority of the DS babies were found to be the 4th child or later born to the same mother.

We also studied the birth weight of the DS children and whether they were born full term. Majority of the DS children (96%) were born full term. Sixty three children (33%) were of normal weight whereas 86 (45%) were above normal birth weight and 42 (22%) were of low birth weight (Figure 2& 3).

Table 1: Socio-Demographics and other characteristics for the participants

Characteristics	Frequency n [%]
Total participants who completed the study	192
Age	
≤ 35	40 [20.83%]
≥ 35	152 [79.16%]
Body Mass Index [BMI]	
Underweight = <18.5	0 [0%]
Normal weight = 18.5–24.9	101 [52.6%]
Overweight = 25–29.9	51 [26.5%]
Obesity = 30 or greater	40 [20.8%]
Education	
Not educated	8 [4.1%]
Primary school	16 [8.3 %]
High school	79 [41.1 %]
Graduates and above	89 [46.3%]
Income	
≤4999 SAR*[equivalent to ≤ 1500 \$]	32 [16.6%]
5000-9999 SAR*[1500-2666 \$]	77 [40.1%]
≥10000 SAR*[≥ 2666 \$]	83 [43.2%]

*SAR is Saudi Arabian Riyal

Table 2: Questions related to participants knowledge of folic acid and its use

Questions	Frequency n [%]
Do you know what folic acid is?	
Yes	151 [78.6%]
No	13 [6.7%]
Not sure	28 [14.5%]
Did you know lack of folic acid causes birth defects?	
Yes	49 [25.5%]
No	62 [32.29%]
Not sure	81 [42.18%]
Did you take Folic Acid When you were pregnant?	
Yes	136 [70.8%]
No	39 [20.3%]
Sometimes	17 [8.8%]
If yes, When?	
Before conception	14[9.2%]*
After Conception	139 [90.8%]*
Length of use of Folic Acid	
A month or morebefore conception	12[7.8%]*
After pregnancy Confirmation [1-2 month later]	38[24.8%]*
Three- or more month later	105[68.6%]*
Did your husband take folic acid	
Yes	5 [2.6%]
No	187 [97.3%]
Did your mother take folic acid	
Yes	2[1.04%]
No	190[98.9%]
Did you consider prenatal testing?	
Yes	5[2.6%]
No	187[97.3%]
Did you take iron	
Yes	179[93.2%]
No	13[6.7%]
If yes, When did u start?	
Before Conception	3 [1.6%]**
1 st trimester	8 [4.4%]**
2 nd trimester and above	168 [93.8%]**

*The percent is calculated from among the total women who had taken folic acid [n=153].

** The percent is calculated from among the total women who had taken iron [n=179].

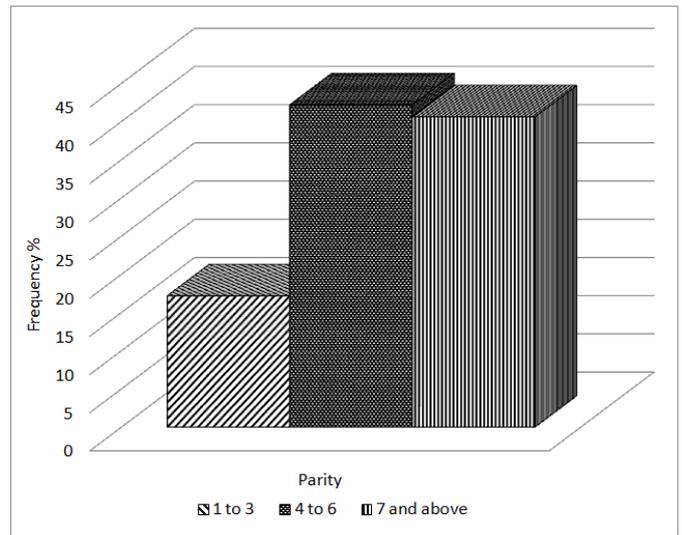


Figure 1: Shows the frequency of participants having Down syndrome child in relation to parity

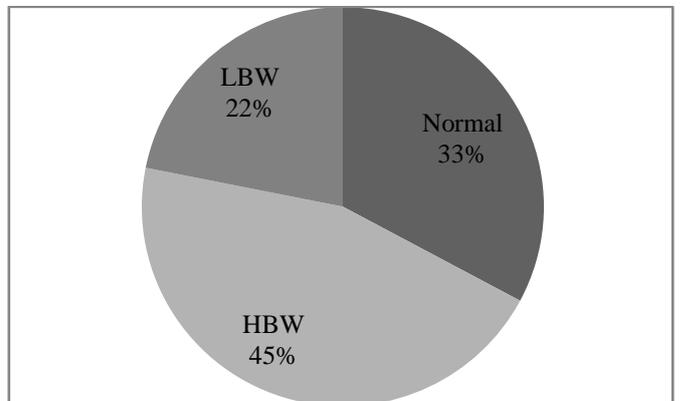


Figure 2: Shows the birth weight of the babies born with Down syndrome

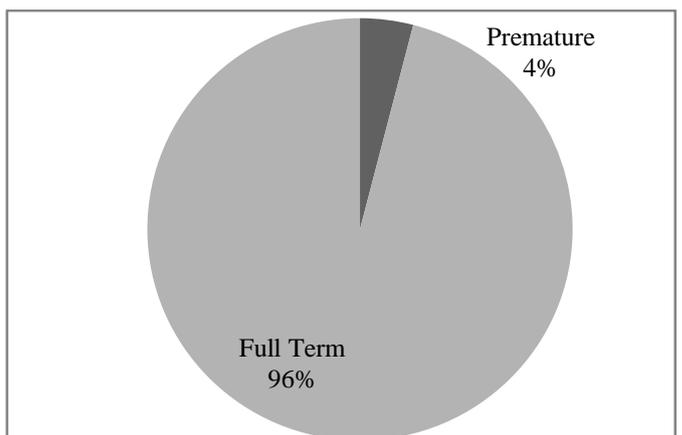


Figure 3: Shows whether the percent of babies born with Down syndrome were full term or preterm.

4. Discussion

Birth abnormalities like Down syndrome and neural tube defects are the most common birth defects across the world. Both types of disorders have a common etiological pathway related to folic acid metabolism [2].

In this study, we have investigated the possible association the women’s folic acid status at the time of

pregnancy may have had with the occurrence of DS. Adequate folic acid status is crucial for the normal chromosome segregation before conception and for post conception closure of the neural tube. A low folic acid status has also been proved to be linked to abnormal homocysteine metabolism leading to higher blood concentrations of homocysteine, thereby, increasing risks for atherosclerosis and other cardiovascular diseases [18;19].

Majority of the women, in this study, with a DS child were aware of the importance of folic acid supplementation but were not sure that its deficiency could cause serious birth defects including Down syndrome and Neural tube disorders especially to the children being born to older ladies (≥ 35 years). Although, there was a high prevalence of folic acid intake among the participants, the majority did not take it at the right time. Proper preconceptional time to start folic acid supplements for the prevention of Down syndrome or any Neural tube defect was not known to the participants and only 9% knew and followed the recommendations. Some women just ignored folic acid supplementation even when aware of benefits. Not many women across the globe know the best timing of the folic acid supplementation, for example, in Norway, only 0.4% of participants knew folic acid should be taken early in pregnancy, whereas, in USA, 7% of the studied population knew the best time to prevent birth defects by taking folic acid supplementation [20;21]. In United Arab Emirates, 79.1% women had heard about folic acid and 66.7% knew about the link between folic acid and birth defects [20]. Daltveit (2004) also reported 33% of the studied population were aware of folic acid's role in pregnancy yet only 10% took the supplements [22].

In the present study, social status or educational background did not play a role in women's awareness of folic acid's importance and its link with birth defects. Almost all the participants had unplanned pregnancies, and were less prepared to take any supplements in the beginning. It is highly recommended that physicians and practitioners urge all women of child bearing age to have adequate preconceptional intake of folic acid between 400 to 1000 μg per day [19]. The prevalence of DS was found to increase among older women [≥ 35 years] as did parity. Many women probably learned about folic acid after becoming pregnant or after visiting the gynecologist, decreasing their chances of supplementation before pregnancy.

Older the mother at conception, higher the risk factor for trisomy-21 and after thirty five years the risk increases proportionally to maternal age [13;23]. But cases of DS also occur in children born to mothers aging less than 35 years for which different mechanisms and factors seem to play a role in chromosome-21 non-disjunction in younger women when compared to older women. Less than 5% of DS cases are due to errors occurring during paternal meiosis but not much is known about the effect of paternal nutrition and aneuploidy in sperms. Though, it has been observed that men with high folate intake had lower frequency of sperm with disomy-21 as

compared to men with lower intake [13;24]. In our study, close to 97% of the fathers did not take folic acid and their diet and eating habits are also not known. Similarly, when asked about the mothers of participants [grandmothers of DS children], almost 99% did not take any supplementation during their pregnancy time. This could have been due to lack of knowledge, awareness and lesser access to clinic during the time. The question arises that why the DS incidences have increased many folds compared to older generations who also did not take folic acid supplementation or were aware of. It may be best answered by the fact that our diets and eating habits have changed drastically that have started to take a toll not only on ourselves but on the next generations to come.

Maternal methyl donor during gestation can alter the offspring phenotype by methylating the epigenome, making it more likely for the grandmother with low folic intake or any disorder in folic acid metabolism during gestation to alter the methylation pattern of several chromosome regions, therefore resulting in an increase in the formation of aneuploidy gametes [13]. Not many studies address the possible role of paternal and maternal grandmother's dietary habits to chromosome-21 non-disjunction. Such controlled studies are very much needed to throw some light and better understand the drastic effects and risks diets may have on the current generation and the generations to come. This becomes even more important when fast foods, which are usually nutrients deficient, have become a norm in most people's lives affecting a large percentage of overall population.

Some studies also suggest that risk of DS may also be related to advanced age of grandmothers [25], but when asked about grandmothers age at the time of participants birth, majority could not answer. Thus, the question was excluded from the study. Agopian *et al* (2012) reported that even young fathers had a higher risk for trisomy-21 in offsprings when the paternal grandmother was older at the time of conception of the father [26].

According to Czeizel and Puho (2005), folic acid and iron had significant protective effect against DS during the first month of pregnancy, and a lower consumption of both these nutrients was reported by mothers of DS off springs in their study. The protective effect was found with the use of iron and folic acid together as well as iron alone [27]. However, in our study, majority of the participants took iron in the second trimester rather than in the beginning of gestation. Since iron is generally prescribed by doctors in the second trimester. The absence of both of these micronutrients could be a potent risk factor for DS among the mothers. There are not many studies that have looked at the direct link of just iron supplementation during preconception and gestation on the prevention of DS but its importance cannot, certainly, be ruled out.

There are also reports about a positive association between parity and Down syndrome in both younger (less than 35 years) and older (more than 35 years) women [10;28]. Women with higher parity (>3) are also less likely to undergo

prenatal screening for DS, and thus are less likely to terminate a DS pregnancy as compared to women of lower parity [10;29]. In this study, we observed a higher frequency of DS births fourth child onwards, which is consistent with previous studies mentioned[5]. So, the higher parity is clearly being the contributing factor in giving birth to the DS child regardless of their folic acid status.

The main limitation of this study was that it was conducted in only one city of Saudi Arabia and can't be generalized to other areas. Another limitation is the reliability of information and recall bias since all responses were self-reported. The dose of folic acid supplementation was also not assessed, since the majority did not take folic acid in the initial gestational period or prior to pregnancy. The strength of the study was taking into account different factors among which anyone or all together could be the cause of DS births among the women.

It's important that men and women become more aware of the importance of folic acid. More health campaigns are needed to increase knowledge about preconceptional use of folic acid and even iron together. Doctors and dieticians should urge all women of child bearing age to consume both folic acid and iron. Since cooking decreases folic acid in the food, other sources should be looked into, like mandatory food fortification of staple foods. That way, even if campaigns and awareness are unable to reach everyone, the majority will have access to folic acid in their foods. In the United States of America, the food drug administration has already recommended the addition of folic acid to enrich grain products since 1986, and was made mandatory by 1998 [18;30]. Such policies should be implemented in all developing countries as well to reduce the occurrence of Down syndrome.

Most of the women we followed were aware of folic acid, but only a few knew about its possible role in preventing DS and other birth abnormalities, and thus were less likely to take folic acid preconceptionally, thus once again emphasizing on the need for more awareness programs regarding the spread of knowledge in the importance of folic acid and its use during pre- and during pregnancy.

Ethical approval

The study was approved by the IRB and ethics committee of the College of Applied Medical Sciences, King Saud University, Riyadh, Saudi Arabia.

Source of Funding

The authors extend their appreciation to the Research Center, College of Applied Medical Sciences and the Deanship of Scientific Research at King Saud University for funding this research.

Conflicts of interests

None declared.

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