Original Article

Maternal Preconception intake of Folic Acid in Malta

Miriam Gatt, Marika Borg, Elaine Grech Mercieca, Neville Calleja

Abstract

Background: Neural tube defects (NTDs) are serious birth defects arising from abnormalities in neural tube development during early embryogenesis. Research shows that taking folic acid prior to and throughout the first 12 weeks of pregnancy will significantly decrease the occurrence of NTDs. The prevalence of NTDs in Malta is 10.0/10,000 births, yet this rate can be brought down to 5.0-6.0/10,000 births with preconception folic acid. This study aims to investigate the maternal intake of preconception folic acid in Malta.

Methods: The National Obstetric Information System (NOIS) collects detailed demographic, pregnancy, delivery and infant outcome data on all births in Malta. One of the variables recorded at the first antenatal visit is whether the mother took folic acid prior to pregnancy. NOIS data for 2015 was obtained, Excel and SPSS were used for analysis.

Results: 4385 women delivered a baby in 2015, of these 1125 (25.7%) reported taking folic acid before pregnancy. Both univariate and multivariate logistic regression showed that maternal age, parity, education, nationality, locality of residence, marital status, planned pregnancy and use of artificial reproductive technology were all significantly associated with taking preconception folic acid ($p<0.001$).

Conclusion: Although preconception folic acid supplementation has been advised since the early 1990s, in Malta only a quarter of mothers are taking this before pregnancy. This low compliance is also documented in other countries. Several maternal factors have been found to be associated with better intake of preconception folic acid. Effective methods of increasing maternal preconception intake of folic acid are necessary to decrease the rate of NTDs in Malta.

Key words

folic acid, neural tube defects, preconception, pregnancy

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Background

Neural tube defects, namely anencephaly and spina bifida, occur at an overall rate of 9.83/10,000 births in Europe with a livebirth rate of 2.61/10,000 livebirths.[1] These are severe, debilitating birth defects responsible for causing significant morbidity and mortality. Folic acid is known to be important for the normal development of the neural tube in early embryogenesis and its effects have been widely investigated. In 1991, a landmark multicentre double blind randomised control study conducted by the Medical Research Council conclusively showed that taking folic acid in the peri-conceptional period (i.e. from one month before conception through to 12 weeks after conception) effectively prevents the occurrence of neural tube defects by up to 50-70%.[2] It has since been documented in several other studies that taking folic acid at the correct time can significantly

decrease the occurrence of neural tube defects.[3]

This knowledge prompted countries worldwide including the UK and USA to issue recommendations as early as 1992 for all women of childbearing age to take regular folic acid supplements.[4,5] In spite of these recommendations and accompanying health promotion initiatives, it was found that whilst women's knowledge and awareness of the benefits of folic acid had increased significantly, its use in the peri-conceptional period had not increased to the desired levels and many mothers were still not taking preconception folic acid. More importantly, the occurrence of neural tube defects had not decreased significantly.[6]

Within this scenario, a number of countries introduced mandatory food fortification of flour to ensure that women were taking the required amounts of folic acid before and during the early weeks of conception. These initiatives have translated into a significant decrease in neural tube defects in those countries having implemented mandatory food fortification with folic acid, whilst these benefits have not been seen in countries without mandatory fortification.[7]

Europe has not introduced mandatory food fortification with folic acid for several reasons including reasons of protecting personal choice and fear of possible negative health effects associated with widespread population intake of folic acid, although the latter have not been confirmed.[8] Europe, including Malta, therefore currently relies on initiatives such as recommendations, health promotion campaigns and women's voluntary supplementation with folic acid preconceptionally.

The total prevalence rate of NTDs in Malta is 11.14/10,000 births with a livebirth rate of 9.0/10,000,[9] yet it has been documented that the rate of non-preventable NTDs can be brought down to 5-6/10,000 births when folic acid is taken correctly in the preconception period.[10]

Health professionals in Malta generally follow UK NICE guidelines in their practice. These guidelines recommend that women of childbearing age take '*400 micrograms daily before pregnancy and throughout the first 12 weeks, even if they are already eating foods fortified with folic acid or rich in folate'.*[11]

This study aims to investigate the current maternal intake of preconception folic acid in Malta and the factors associated with an increased probability of the mother taking preconception folic acid.

Methods

Detailed medical birth data on all deliveries and births on the Maltese Islands are collected on a routine basis by the National Obstetric Information System (NOIS) of the Directorate for Health Information and Research (DHIR). This is the official medical births data source of Malta. Detailed demographic, pregnancy, delivery and outcome data for all births of 22 weeks gestation and over is collected at the obstetrics units from the hospital medical records and forwarded to the DHIR where the data is checked, validated and entered into the NOIS database.

At their first antenatal clinic visit at hospital, women are routinely asked whether they have been taking folic acid supplements and whether they started them before pregnancy. For the period between 1st January and 31st December 2015 this data was inputted into the NOIS database. Anonymous data on mothers' reported preconception folic acid intake together with maternal age, parity, marital status, education, nationality, locality of residence, planned pregnancy and use of assisted reproductive technology (ART) for the year 2015 was extracted from the NOIS database and used for this retrospective registry based study. Maternal nationalities were grouped into 5 categories reflecting the maternal geographic region of origin: i) Malta, ii) countries which joined the EU pre-2004 and EFTA countries, iii) other European countries, iv) Africa or Middle East and v) all others. Maternal locality of residence was categorised into 6 districts according to the system of Local Administrative Units (LAUs) created by EUROSTAT which is compatible with the Nomenclature of Territorial Units for Statistics (NUTS).[12]

Excel and SPSS were employed to analyse the data using chi-square and multivariate logistic regression analysis.

***Table 1**: Characteristics of mothers and their reported preconception folic acid intake*

Maternal Character-istic	Categories	Total Number of mothers	Preconception Folic acid taken	% (95% CI) of mothers taking Folic acid preconception	Chi-Square value	Degree of freedom	*P-value*
Total		**4385**	**1125**	**25.7 (24.4-27.0)**			
Age	<25	640	45	7.0 (5.5 - 9.4)	92.6	2	**p<0.001**
	25-35	3126	908	29.0 (27.5-30.7)			
	>35	619	172	27.8 (24.3-31.5)			
Nationality	Maltese	3544	998	28.2 (26.7-29.7)	59.5	4	**p<0.001**
	EU pre 2004 & EFTA	217	45	20.7 (25.7-26.9)			
	Other European	242	48	19.8 (15.1-25.5)			
	Africa & Middle East	281	12	4.3 (2.3 - 7.5)			
	Others	98	22	22.4 (14.9-32.2)			
Locality of maternal residence	North	789	216	27.4 (24.3-30.7)	37.2	5	**p<0.001**
	Western	548	196	35.8 (31.8-40.0)			
	N.Harbour	1332	307	23.0 (20.8-25.4)			
	S.Harbour	719	132	18.4 (15.6-21.4)			
	South East	705	210	29.8 (26.6-33.3)			
	Gozo	292	64	21.9 (17.2-26.7)			
Completed level of Education*	Tertiary	1481	556	37.5 (35.1-40.1)	93.6	2	**p<0.001**
	Vocational/ non-tertiary	1047	279	26.7 (24.0-29.5)			
	Secondary	1629	281	17.2 (15.5-19.2)			
Marital Status	Married	3009	977	32.5 (30.8-34.2)	150.8	2	**p<0.001**
	Single	1197	120	10.0 (8.4 -11.9)			
	Separated/ divorced	179	28	15.6 (10.8-22.0)			
Parity	Nulliparous	2223	703	31.6 (29.7-33.6)	50.0	1	**p<0.001**
	Multiparous	2162	422	19.5 (17.9-21.3)			
Planned Pregnancy*	Yes	2884	1074	37.2 (35.5-39.0)	325.5	1	**p<0.001**
	No	1216	40	3.3 (2.4 – 4.5)			
ART	Yes	97	63	64.9 (54.5-74.2)	36.4	1	**p<0.001**
	No	4288	1062	24.8 (23.5-26.1)			

**Cases with maternal characteristic not reported excluded from analysis*

Table 2: *Odds Ratios for univariate and multivariate logistic regression for characteristics of mothers and associated preconception folic acid intake*

Characteristic	Categories	UNIVARIATE OR (95% CI)				ADJUSTED OR (95% CI)			
		OR	**Lower CI**	**Upper CI**	***p*-value**	**Adj OR**	**Lower CI**	**Upper CI**	***p*-value**
Age	25-35yrs	1.00			***p*<0.001**	1.00			***p*<0.001**
	<25yr	0.18	0.14	0.25		0.44	0.31	0.63	
	>35yr	0.94	0.78	1.14		1.24	0.98	1.56	
Nationality	Maltese	1.00			***p*<0.001**	1.00			***p*<0.001**
	EU pre2004 & EFTA	0.67	0.48	0.93		0.78	0.53	1.15	
	Other European	0.63	0.46	0.87		0.54	0.38	0.78	
	Africa & Middle East	0.11	0.06	0.20		0.10	0.05	0.22	
	Others	0.74	0.46	1.19		0.55	0.32	0.94	
Locality of maternal residence	North	1.00			***p*<0.001**	1.00			***p*<0.001**
	Western	1.48	1.17	1.87		1.26	0.96	1.65	
	N.Harbour	0.79	0.65	0.97		0.99	0.79	1.26	
	S.Harbour	0.60	0.47	0.76		0.80	0.60	1.06	
	South East	1.13	0.90	1.41		1.18	0.91	1.54	
	Gozo	0.74	0.54	1.02		0.49	0.35	0.70	
Completed level of Education	Tertiary	1.00			***p*<0.001**	1.00			***p*<0.001**
	Vocational / non-tertiary	0.60	0.51	0.72		0.77	0.63	0.94	
	Secondary	0.35	0.29	0.41		0.62	0.51	0.75	
Marital Status	Married	1.00			***p*<0.001**	1.00			***p*<0.001**
	Single	0.23	0.19	0.28		0.46	0.36	0.59	
	Separated /divorced	0.39	0.26	0.58		0.51	0.32	0.81	
Parity	Nulliparous	1.00			***p*<0.001**	1.00			***p*<0.001**
	Multiparous	0.52	0.46	0.60		0.50	0.43	0.59	
Planned Pregnancy	No	1.00			***p*<0.001**	1.00			***p*<0.001**
	Yes	17.45	12.62	24.12		11.87	8.52	16.55	
ART	No	1.00			***p*<0.001**	1.00			***p*<0.001**
	Yes	5.63	3.69	8.59		2.67	1.67	4.29	

Results

A total of 4385 women delivered a baby of 22 weeks gestation or over in 2015, of these 1125 (25.7%) women reported having taken folic acid before pregnancy.

Table 1 presents a comparison of mothers having reported taking preconception folic acid and others not having taken preconception folic acid according to various maternal characteristics with the level of significance. Maternal age, parity, education, nationality, locality of residence, marital status, pregnancy planning and use of ART were all found to be very significantly associated ($p<0.001$) with use of preconception folic acid supplementation.

Multivariate logistic regression showed that all parameters tested were independently associated with the likelihood of having or not having taken preconception folic acid (Table 2). Results showed that women having had a planned pregnancy or having undergone ART were the most likely to take preconception folic acid with adjusted odds ratios of 11.87 (95% CI 8.52-16.55) and 2.67 (95% CI 1.67-4.29) respectively (Table 2).

Low educational level, multiparity, unmarried mothers, mothers younger than 25 years and foreign mothers (i.e. Non-Maltese and non-EU pre-2004/EFTA nationality) were independently, significantly associated with a lower likelihood of taking preconceptional folic acid.

Analysis of maternal locality of residence by region was also significantly associated with taking supplemental folic acid preconceptionally, with Gozitan women reporting taking significantly less folic acid before pregnancy than women residing in other areas.

Discussion

In spite of the long-term knowledge of the benefits of preconception folic acid, only a quarter (25.7%) of the mothers delivering in Malta reported having taken folic acid before pregnancy. This rate is too low to avoid all potentially preventable NTDs. Similar undesirably low rates have been documented in several other European countries.[13]

In this study, higher maternal educational level was found to be significantly associated with increased preconception folic acid intake. Similar findings have been documented in other studies. A study from the Netherlands in 2008 found that while 31% of women with low educational level had taken peri-conceptional folic acid supplements, 63% of women with a high educational level had taken preconception supplementation.[14] A more recent Italian study of over 2189 women by Nilsen at al. (2016) reported that 9.4% of mothers with low educational level took preconception folic acid compared to 31.1% of mothers with a tertiary education level.[15]

Similar to other studies, young women were found to be the least likely to take folic acid supplementation preconceptionally, with only 7.0% of mothers in Malta aged less than 25 years taking preconception folic acid.[16] Furthermore, nulliparous women were found to be more likely to take preconception folic acid than multiparous women as also found in other studies.[17] In our study, mothers of African or European non-EU origin were associated with the lowest rates of preconception folic acid intake. This highlights the possibility of existent health inequalities and issues with health promotion messages and recommendations reaching foreign mothers and mothers of minority ethnic groups. In the UK, a study of nearly half a million pregnant women by Bestwick et al. (2014) also describes a troubling situation where non-Caucasian women were far less likely to take folic acid before pregnancy, a situation, they conclude, which is leading to health inequalities.[18]

Understanding the characteristics of women least likely to take folic acid preconceptionally can inform policy to better target initiatives aimed at increasing women's preconception folic acid intake. Any initiatives undertaken must ensure that they effectively reach those categories of women identified as being less likely to be taking folic acid in the recommended period, avoiding inequalities between women of different socioeconomic status.[19]

While Health Promotion campaigns are often considered the first line intervention to affect a change in behaviour, research has shown that non-targeted campaigns have been of limited success in increasing women's intake of folic acid. A systematic review investigating the rates of preconception folic acid uptake in various countries before and after health promotion campaigns shows that the rate of uptake following intervention varies and increased on average from 14 to 23%.[20] These disappointing results indicate that health promotion campaigns have not been successful in satisfactorily changing women's behaviours.[14,21] It has been

suggested that alternative interventions including health-care based interventions such as making folic acid supplements easily available may be found more effective in the longer term than using mass media or printed resources in isolation.[19]

Pregnancy planning and undertaking assisted reproduction were found to be the characteristics most significantly associated with increased maternal intake of folic acid. These associations have also been described elsewhere and indicate that an effective way of increasing peri-conceptional folic acid intake might be to improve family planning by providing appropriate clinics.[15]

Women's knowledge and intake of folic acid supplements is influenced significantly by health care professionals' advice, namely general practitioners, obstetricians, paediatricians and pharmacists.[22] General practitioners have an important role in increasing awareness and improving preconceptional folic acid intake. It is important that they are aware of this and give appropriate advice to all women of childbearing age even when they are attending clinics for other reasons. Unfortunately, it has been documented that a number of family doctors are themselves not fully aware of the benefits and correct timing and dosage of peri-conceptional folic acid intake.[23] Although obstetricians are fully aware and do provide folic acid supplementation advice, women generally present at the obstetricians' clinics following conception, at a time too late for prevention of potentially avoidable NTDs. Post-natal clinics could also provide a venue for educating and informing women of the benefits of folic acid for future pregnancies. Other sources of information on the importance of folic acid include the media, family and friends. Our data did not have data on maternal sources of folic acid knowledge and this could not be studied for the local scenario.

Preconception clinics have been implemented in several countries with the aim of improving pregnancy and infant outcomes.[24] The Italian study by Nilsen et al. (2016), reported that the adjusted prevalence ratio of taking preconception folic acid for women intending to get pregnant who attended a health visit prior to conception was 7.90 (95% CI 4.62-13.5), compared to 2.87 (95% CI 1.72-4.79) for women with pregnancy intention but not having attended a preconception health visit.[15] Women suffering from diseases needing pregnancy planning have also been found to be significantly more likely to take preconception folic acid with an adjusted odds ratio of 1.7 (95% CI 1.2-2.5).[16] Preconception clinics are ideal venues that may educate and encourage women to take preconception folic acid supplements, however, such clinics are not available in Malta.

Limitations of this study include the fact that folic acid uptake relied on maternal reporting and the actual uptake of folic acid may be lower than that reported due to maternal non-compliance and their reluctance to report this. Additionally, the doses and exact timing of folic acid supplementation were not available and could not be assessed.

Conclusion

In the absence of mandatory food fortification, countries must be innovative and pro-active in undertaking initiatives to improve women's folic acid uptake with the aim of avoiding potentially preventable devastating birth defects as are neural tube defects. This is an area which undisputedly offers great public health potential. It is important to ensure that any initiatives undertaken reach all maternal categories including the more vulnerable women. Having local research determining women's views of the barriers and enablers to the uptake of preconception care and peri-conceptional folate supplementation may also go a long way in directing effective policy making in this area.

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