

Global Diversity in Acceptability of Vaccines during Pregnancy

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ABSTRACT

Objective: Due to lack of information regarding attitudes and behaviors of pregnant women towards vaccines, we sought to study the acceptability of influenza, pertussis and a hypothetical Group B Streptococcus (GBS) vaccine during pregnancy from a global perspective.

Method: Data were abstracted from responses of 782 pregnant women from North America, Europe and Brazil to an industry sponsored online survey in 2014. Participants were provided brief disease and vaccine synopses prior to completing the survey.

Results: Significant differences in vaccine acceptance were observed across regions and vaccine types. Women from Brazil had the highest rate while those from Europe had the lowest rate of acceptance for all vaccines. For all regions and all vaccine types, physician recommendation positively influenced patient acceptance of vaccines ($p < 0.05$). The GBS vaccine was the highest rated for vaccine acceptance globally. Neonatal protection was a significantly stronger motivator compared to self-protection for each region and vaccine type. Working status, income, parity and compliance with medical care were significantly associated with vaccine acceptance but in an inconsistent manner for region and vaccine type. Health care providers were considered as the most credible source and medical and pregnancy specific websites were considered the most credible online source of pregnancy related information across all regions.

Conclusion: Understanding regional differences in the acceptability of vaccines among pregnant women, effective use of the internet and most importantly involvement of the physician in disseminating vaccine related information to the public is key to increasing the uptake of vaccines during pregnancy.

Keywords: Group B Streptococcus, Pregnancy, Global diversity, Vaccine

Abbreviations: GBS: Group B Streptococcus

INTRODUCTION

Vaccination is a well-established health prevention strategy that reduces the burden of a number of infectious disease conditions worldwide. This approach has gained strong acceptance within pediatric populations, but has lagged behind for adults due to a variety of reasons. Among these is a poor understanding of the importance of adult vaccination and logistical concerns such as vaccine access and cost. In pregnancy, recent efforts have contributed to the establishment of a specific maternal vaccine platform. The intention of these developments is to help reduce the disease burden for several vaccine-preventable pathogens in both the mother and neonate [1-17]. However, additional barriers in this special population such as limited or no experience of health care providers and the lack of pregnancy-specific clinical trials data raises concerns about potential long term sequelae for the child, further limiting progress on maternal immunization efforts [8,18-21].

There is a paucity of information currently available regarding knowledge, behavior and attitudes of pregnant women concerning vaccination during pregnancy. These are even less understood from a more global perspective. Understanding global differences in the uptake of vaccines in pregnant women is of particular importance, given the fact that clinical trials are often run internationally but once licensed; vaccines are used across national boundaries. Additionally, increasing number of countries have a regular

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influx of immigrant women who are pregnant, requiring an improved sensitivity toward local customs and behaviors as these patients are incorporated into their newly adopted health care communities.

We had the unique opportunity to examine globally acquired data extracted from an industry sponsored patient survey to address some of the above issues. We opted to examine three vaccines, two of which are already commercially available and one is a hypothetical vaccine in development. The influenza vaccine was selected because of the anticipated well-recognized disease burden and long established recommendation for use in pregnancy. This vaccine has been supported primarily for its benefit to maternal health, although benefits to the neonate have also been reported [8-12]. The second vaccine, the pertussis vaccine, is less recognized for its disease burden in adults and to the newborn, and has only recently been advocated for use in pregnancy. Although benefits to the mother from pertussis vaccination are identifiable, the main scope of the current recommendations focuses on protection of the newborn child [14,15]. The last (hypothetical) vaccine is directed against Group B Streptococcus (GBS) and is currently being investigated for use in pregnancy with an exclusive focus on neonatal benefit [22]. We sought to better understand the perspectives of pregnant patients for each of these vaccines and their willingness to receive them during pregnancy.

MATERIALS AND METHODS

A total of 782 women between 12 and 40 weeks of pregnancy from USA, Canada, Brazil, France, Germany, Ireland and the Netherlands participated in a twenty minute online survey in 2014. Written informed consent for participation in the study was obtained from participants. This industry sponsored survey was primarily focused on attitudes and behaviors of pregnant women regarding influenza, pertussis and GBS vaccination during pregnancy. It consisted of five sections with total 54 questions related to general prenatal health behavior, demographic data of participants, acceptability of the three vaccines, motivation for receiving these vaccines and sources of pregnancy related information. Being up-to-date with other vaccines and laboratory testing was considered as being compliant with healthcare. Participants were supplied disease profiles

and vaccine synopses prior to completing the survey (available upon request). Questions related to the acceptability of the three vaccines were answered using a scale of 1 to 10, with 1 being "Not at all likely/strongly disagree" and 10 being "Extremely likely/strongly agree". No exclusion criteria were applied. Willingness to undertake the online survey was the only requirement.

Hierarchical cluster analyses demonstrated that data from countries within each region e.g. countries within Europe as well as countries within North America exhibited similar patterns. Hence, further analysis was performed by grouping data into 3 regions– North America (USA and Canada - 400 women), Europe (France, Germany, Ireland and the Netherlands - 282 women) and Brazil (100 women). Acceptability of vaccines scored on a scale of 1 to 10, was divided into dichotomous variables: A score of 8-10 was considered as an affirmatory response and 1-3 was considered as declinatory response. Mean scores were also calculated for a comparison of acceptability of vaccines.

Descriptive statistical analysis was performed by utilizing a z test for dichotomous variables and a t test for continuous variables. Factors associated with acceptability of vaccines were analyzed using univariate linear and logistic regression analysis. Linear regression models were based on acceptability of vaccines as dependent variable (ranging from 1 to 10) with factors controlled for collinearity. A sample size calculation was not performed in this cross sectional survey study.

RESULTS

A total of 782 surveys were analyzed, of which 400 (51%) were from North America, 282 (36%) from Europe and 100 (13%) from Brazil. Demographic characteristics are listed in **Table 1**. There were no differences in the frequency of young and multiparous participants across the three regions. Brazil differed significantly from other regions in having the highest frequency of women who were working or lived in urban areas and the lowest frequency of women who held university or higher degrees or had a high level of household income. The majority of women in North America and Brazil reported compliance with general health care, but less so in European respondents.

Table 1. Demographic characteristics of participants.

Questions	North America (n=400) %	Europe (n=282) %	Brazil (n=100) %
Age (less than 35 years)	74	72	74
Primiparous	28	32	25
University and higher Education	56	36	20*
Working	56	68	79 *
High household income	79	89	70*
Urban residence	62	50	93 *
Compliant with vaccines and tests even when not pregnant	64	45	79*

Working- full time or part time

High household income- more than \$30,000 per year for North America; more than 4600 reais for Brazil; more than 15000 euros for Europe

**p<0.05 - z test for comparisons between North America, Europe and Brazil*

There were significant differences in vaccine acceptance across regions and vaccine types (**Table 2**). For all vaccines, respondents from Brazil demonstrated the highest levels of vaccine acceptance, and the lowest levels of vaccine refusal. Those subjects from the Europe cohort had the lowest levels of acceptability and the highest refusal rates. For all regions and all vaccine types, a physician recommendation for vaccine administration positively influenced patient

acceptance. Of interest, the hypothetical GBS vaccine was the highest rated for vaccine acceptance globally, differing significantly with the other two vaccines. This was particularly evident in Europe, where after physician recommendation; the GBS vaccine was the only vaccine acceptable to the majority (52%) of respondents in that region.

Table 2. Patient acceptability towards vaccination.

Types of vaccines	Questions	North America (n=400)	Europe (n=282)	Brazil (n=100)
Influenza	Not discussed by doctor			
	Yes (%)	43	14	69*
	No (%)	24	53	13
	Mean score	6.25	3.83	7.77*
	Recommended by doctor			
	Yes (%)	65**	34**	88*,**
	No (%)	11	28	2
	Mean score	7.61**	5.73**	9.17*,**
Pertussis	Not discussed by doctor			
	Yes (%)	50	18	73*
	No (%)	18	43	12
	Mean score	6.76	4.47	7.97*
	Recommended by doctor			

GBS	Yes (%)	65**	37**	89*,**
	No (%)	7	23	1
	Mean score	7.83**	6.05**	9.33*,**
	Not discussed by doctor			
	Yes (%)	49	24	74*
	No (%)	14	38	11
	Mean score	6.85	4.94	8.16*
	Recommended by doctor			
	Yes (%)	66**	52**	91*,**
	No (%)	6	11	3
	Mean score	7.95**	7.1**	9.28*,**

* $p < 0.05$ - comparisons between North America, Europe and Brazil

** $p < 0.05$ - comparisons between "Recommended by doctor" and "Not discussed by doctor" for each vaccine

With regard to motivation for accepting a vaccine type, women were asked for their degree of acceptance related to self-protection against the associated pathogen (**Table 3**). Again, relative differences were noted for each region with Europe expressing the least concern for self-protection across vaccine types and Brazil showing the highest levels of concern. This same relationship was noted for concerns

regarding protection of the baby and vaccine acceptance. Importantly, for each region and each vaccine, neonatal protection was a significantly stronger motivator compared to self-protection. For all vaccine types, concern for neonatal protection against GBS was the most strongly identified motivator for vaccine acceptance.

Table 3. Patient motivation for vaccination.

Types of vaccines	Questions	North America (n=400)	Europe (n=282)	Brazil (n=100)
Influenza	Protection for self			
	Yes (%)	48**	17**	75*,**
	No (%)	21	51	9
	Mean score	6.47**	4.18**	8.31*,**
	Protection for baby			
	Yes (%)	57	37	87*
	No (%)	11	27	2
	Mean score	7.46	5.88	9.19*
Pertussis	Protection for self			
	Yes (%)	54**	22**	78*,**
	No (%)	15	37	5
	Mean score	6.95**	4.8**	8.64*,**
	Protection for baby			
	Yes (%)	64	40	89*
	No (%)	7	20	2

	Mean score	7.85	6.28	9.23*
GBS	Protection for self			
	Yes (%)	48**	27**	81**
	No (%)	15	31	6
	Mean score	6.76**	5.3**	8.67**
	Protection for baby			
	Yes (%)	65	50	90*
	No (%)	8	14	3
	Mean score	7.87	6.97	9.19*

* $p < 0.05$ - comparisons between North America, Europe and Brazil

** $p < 0.05$ - comparisons between "Protection for self" and "Protection for baby" for each vaccine

Using linear and logistic regression analysis, our data showed that multiple demographic and behavior characteristics influenced vaccine acceptance but in an inconsistent manner depending on region and vaccine type (data not shown). Some of the consistent variables

associated with vaccine acceptance included being compliant with medical care in North America, working status and being worried about risk to personal health in Brazil and multiparity in Europe (**Table 4**).

Table 4. Predictor variables significant for acceptability of at least one vaccine by regression analysis.

Region	Variables
North America	Working status
	Keeping current on all vaccines and tests
Europe	Multiparity
Brazil	Working status
	Concern about health risk to self
	University education

Concerning access to vaccine information, regions were relatively consistent with regard to resources utilized (**Table 5**). The overwhelming majority of respondents rely on their health care provider for vaccine information. Although the internet is also commonly accessed, this source of information was not seen as particularly reliable or credible. For internet resources, standard search engines were consistently used across regions, followed by medical and pregnancy-specific websites. These latter two sources of data were seen as the most credible, but lagged substantially behind direct health care provider information.

Table 5. Resources for information on vaccination.

	North America (n=400) %	Europe (n=282) %	Brazil (n=100) %
Who do you consult when you have a question about pregnancy or infant health?			
Health care providers	89	94	93
The internet	59	66	80
Family	57	51	47
Friends	47	43	41
Pregnant women's or mothers' support group	33	19	43
Who is the most credible source of information?			
Health care providers	81	88	88
Family	7	4	2
The internet	5	3	5
	North America (n=237) %	Europe (n=187) %	Brazil (n=80) %
Which internet resources do you use?			
Search engines	90	88	86
Pregnancy-specific websites	65	66	43
Medical websites	68	50	45
Social media	30	15	34
Which is the most credible internet resource?			
Pregnancy-specific websites	32	51	39
Medical websites	46	22	31
Search engines	14	16	23

* Health care providers (Physicians and Midwife/Nurse Practitioner); * Pregnancy-specific websites (e.g. BabyCenter, Pregnancy.com); Medical websites (e.g. WebMD, Mayo Clinic); Search engines (e.g. Google, Bing); Social media (e.g. Facebook, Twitter, Pinterest)

DISCUSSION

The results of this survey demonstrate a relatively strong, positive attitude towards acceptability of the influenza, pertussis and the hypothetical GBS vaccines in North America and Brazil, with more of a restrained response from women in Europe. However, no region in our study achieved a level of acceptability comparable to that anticipated if pediatric vaccination was being discussed [23]. These numbers also fall short of Healthy People 2020 and WHO goals related to adult vaccination [24,25]. Physician recommendation appears to be an important factor in acceptability of vaccines in all regions evaluated. This is consistent with previous studies that have reported increased acceptability to vaccination during pregnancy when a health care provider was involved in the process [19,26,27].

An interesting observation is that women across the world demonstrated increased willingness towards accepting a hypothetical vaccine, such as the GBS vaccine, compared to the better known and licensed influenza and pertussis vaccines during pregnancy. It could well be that there is an inherent curiosity towards a relatively lesser known disease and its vaccine potential among the general public. But more so, an informed choice toward prevention of a deleterious disease of one's neonate with vaccination may be an important driving force in the difference of acceptance rates towards these vaccines. Although a direct causal relationship between the two could not be established, vaccine acceptance during pregnancy to help protect the baby rather than self-appeared to be a higher motivator. This was universally true for women across all regions in our study. A recent online survey from the UK regarding attitudes of

women toward the influenza, pertussis and GBS vaccines demonstrated that despite their lack of knowledge about GBS disease during pregnancy, women were willing to accept the vaccine directed against this pathogen at the same rate as the influenza and pertussis vaccines. In fact, their acceptance of the GBS vaccine further increased by 10% after reading information on the GBS disease condition [21].

This study has demonstrated that there are striking regional variations in acceptability of vaccines during pregnancy despite the fact that the same information regarding these diseases and vaccines was provided to all the study participants. Generally, women in North America accepted all vaccines at similar rates and did not discriminate between the types of vaccines. This likely reflects a general positive attitude toward vaccination in this region. Furthermore, women in North America, who were compliant with their health, were more receptive toward vaccination.

Similarly, there was a strong positive response in favor of all three vaccines among women in Brazil. Along with protection of baby, there was an increase in vaccine acceptability in these women due to concerns of risk to self-health. Thus the very high rate of vaccine acceptance in this region could be a reflection of dual motivation for protecting baby as well as self.

Women vaccine acceptance during pregnancy was the lowest in Europe. Although they followed similar trends toward the desire to protect their neonates via maternal vaccination, their negativity towards vaccine uptake may be reflected in overall attitudes toward health care, in that, these same individuals reported reduced compliance with health related concerns.

Although there were no regional differences in demographic factors like age and parity, women in the study differed with respect to their education, working status, household income and area of residence. These demographic differences were associated with and may have contributed to the regional variations in vaccine acceptance.

Several studies have looked at potential barriers for vaccination. It seems clear that physician knowledge and positive attitude towards vaccination is an important contributor for increasing vaccine uptake among women [19,20,27-33]. Fear of vaccines and lack of disease-related knowledge in the pregnant population have been shown as hindrances to vaccine uptake [34,35]. It is not only the provision of information but also its content that is crucial. For example, women were more willing to accept the influenza vaccine when they were informed about a “two for one” benefit of the vaccine [36]. There is a need for health messages like these to be efficiently conveyed to women.

Communication strategies to improve vaccination rates among pregnant women are being evaluated with randomized controlled trials [37-39]. Patient targeted educational interventions through verbal discussion,

information pamphlets, and text messaging [35,37,40-42] have made moderate improvements in vaccination uptake rates in regional studies, yet there is a need for continued efforts to achieve additional advancements on a more global level. Our study demonstrated that the internet was the second most common resource that many women relied upon for pregnancy related information. Updating medical websites with maternal immunization topics and using the internet as a means of propagation of relevant vaccine information, their availability and cost should be a focused initiative. Although these resources were viewed by many participants in our study as credible to obtain health related information, health professionals were still prioritized as the most reliable resource. Thus, dissemination of relevant risk vs. benefit information of maternal immunization towards fetal and neonatal disease prevention by health care providers remains key to increasing vaccine uptake among pregnant women globally. Most importantly, understanding regional variations during such efforts may yield better results than the adoption of universal policies and campaigns to promote the use of vaccines during pregnancy.

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DISCLOSURE

Novartis Vaccines and Diagnostics, Inc. provided unrestricted access to the global survey database referred to in this paper and also provided financial support for the independent statistical analysis of data cited on this manuscript. On March 2, 2015, GlaxoSmithKline completed acquisition of Novartis Vaccines Non-flu vaccines business and now owns the data cited.

CONSENT TO PARTICIPATE

Written informed consent for participation in the study was obtained from participants.

ETHICS APPROVAL

We have used already existing data that has no identifiers attached.

This falls under the Exemption categories according to Wayne State University IRB.

CONSENT TO PUBLISH

Not applicable

COMPETING INTERESTS

The authors declare that they have no competing interests. Authors' Contributions: MP and BG have made contributions to conception and design of the study entirely, participated in analysis and interpretation of data. MP has been involved in drafting the manuscript and along with BG has revised it critically for important intellectual content; both have given final approval of the version to be published.

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