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Rubella immunity among pregnant women aged 15–44 years, Namibia, 2010☆

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SUMMARY

Background: The level of rubella susceptibility among women of reproductive age in Namibia is unknown. Documenting the risk of rubella will help estimate the potential burden of disease in Namibian women and the risk of congenital rubella syndrome (CRS) in infants, and will guide strategies for the introduction of rubella vaccine.

Methods: A total of 2044 serum samples from pregnant Namibian women aged 15–44 years were tested for rubella immunoglobulin G antibody; the samples were obtained during the 2010 National HIV Sentinel Survey. The proportion of women seropositive for rubella was determined by 5-year age strata, and factors associated with seropositivity were analyzed by logistic regression, including age, gravidity, HIV status, facility type, and urban/rural status.

Results: Overall rubella seroprevalence was 85% (95% confidence interval (CI) 83–86%). Seroprevalence varied by age group (83–90%) and health district (71–100%). In the multivariable model, women from urban residences had higher odds of seropositivity as compared to women from rural residences (odds ratio 1.40, 95% CI 1.09–1.81).

Conclusions: In the absence of a routine rubella immunization program, the high level of rubella seropositivity suggests rubella virus transmission in Namibia, yet 15% of pregnant

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Namibian women remain susceptible to rubella. The introduction of rubella vaccine will help reduce the risk of rubella in pregnant women and CRS in infants.

Keywords

Rubella; Seroprevalence; Namibia; Pregnant women; Population immunity

1. Introduction

Rubella is a vaccine-preventable viral disease that is characterized by a febrile illness and rash.[1] Rubella infection in pregnant women can lead to congenital rubella syndrome (CRS), which can result in severe illness, disability, and death in the fetus.[2] Worldwide, more than 100 000 children are born each year with CRS.[3,4]

From 2000 to 2009, reported rubella cases increased 20-fold in the World Health Organization (WHO) African Region.[5] Despite this increase in reported number of cases, as of 2015, there is no rubella elimination, control, or prevention goal in the African Region.[4] Thus far, a small number of Sub-Saharan African countries have introduced rubella-containing vaccine in their Expanded Programme on Immunization (EPI) childhood immunization schedule (Burkina Faso, Ghana, Rwanda, Senegal, and Tanzania), and others are planning to do so in the next few years.[1]

The WHO recommends that countries without rubella vaccine assess the burden of rubella and CRS.[6] Serosurveys have suggested rubella virus circulation in a number of African countries,[7] but no published studies have investigated seroprevalence in Namibia. Currently, rubella-containing vaccine (RCV) is not available publicly in Namibia. Understanding the level of rubella susceptibility in pregnant women in Namibia will provide important information to help determine the burden of disease and the need for the introduction of rubella vaccine.[8]

Namibia is a country in southwestern Africa that gained independence from South Africa in 1990. It has an estimated population of 2.1 million.[9] The capital city is Windhoek, and the country is administratively organized into 34 health districts in 14 regions, including those with the highest populations in the northern part of the country along the border with Angola, and in the central and the southern parts of the country.[10] The majority (57%) of Namibian residents are rural dwellers.[9] In 2014, Namibia had one of the highest HIV prevalence rates for adults aged 15–49 years in the world at 16.0%;[11] overall prevalence was high compared with other countries in the Sub-Saharan Africa region.[12] The total fertility rate has been estimated at 3.1 per woman and the crude birth rate at 26 per 1000 population.[13]

To evaluate rubella immunity in pregnant women 15–44 years of age and examine factors associated with seropositivity, stored serum samples from the 2010 Namibia National HIV Sentinel Survey were tested. Rubella immunoglobulin G (IgG) antibody seroprevalence estimates will provide evidence to support the decision to introduce rubella vaccine as part of the Namibia national EPI and to guide efforts to prevent rubella and CRS.

2. Methods

In 2010, the Namibia Ministry of Health and Social Services (MoHSS) conducted a nationwide sentinel survey to estimate HIV prevalence in pregnant women aged 15–49 years. The survey was designed using the standardized WHO methodology for HIV prevalence surveys, using convenient consecutive sampling of women attending antenatal clinics (ANC) selected based on geographic representation from all regions and health districts, urban and rural clinics, areas with different population densities and sizes, and women of different socioeconomic status.[14,15] All pregnant women aged 15–49 years were included in the survey if they attended an ANC for the first time during their current pregnancy, were not referred from another health facility, and agreed to a routine blood draw.

The 2010 survey enrolled 7983 pregnant women from all 34 health districts, 35 main hospitals, and 93 satellite health centers and clinics; 7888 (98.8%) of the enrollees had specimens collected during March 22 to September 6, 2010.[15] Unlinked, de-identified specimens were tested for HIV antibodies. All de-identified data fields (unique identification, district abbreviation and site number, facility type, date of ANC visit, woman's age, gravidity, place of residence, antiretroviral therapy participation, and counseling for prevention of maternal-to-child transmission) were retained electronically. Specimens were stored at 4–8 °C at the Namibia Institute of Pathology in Windhoek.

To estimate the prevalence of rubella IgG antibody within each 5-year age group, it was determined that 428 specimens in each age group would be necessary, assuming seroprevalence of 50%, desired precision of ±5%, probability of achieving the desired precision of 0.95, and 10% loss due to specimens not found or inadequate. There were too few specimens in the 45–49 years age stratum for meaningful estimates, so these samples were excluded. The number of specimens in the 40–44 years age stratum was less than the targeted number, so all specimens were sampled. To control for the distribution of HIV-infected women within each age group, the target sample size was allocated to the HIV-positive and HIV-negative groups based on their observed distributions in the sentinel survey.[15]

Testing for rubella IgG antibody was performed by the Namibia Institute of Pathology in 2012, using an enzyme immunoassay (EIA) to detect rubella-specific IgG (Enzygnost; Siemens, Germany); tests were performed in accordance with the manufacturer's recommendations. Samples with corrected optical density (OD) values >0.2 were considered positive, samples with values <0.1 were considered negative, and samples with values of 0.1–0.2 were considered equivocal. Specimens that tested equivocal were retested as per the manufacturer's instructions, and if the result was confirmed, samples were classified as equivocal, otherwise as positive or negative. To monitor the performance of the EIA, an in-house positive control for rubella IgG antibody was included on every EIA plate in addition to the controls supplied by the manufacturer. A 5% random sample of specimens were tested at the US Centers for Disease Control and Prevention (CDC, Atlanta, GA, USA) for quality assurance; high concordance was found with the testing at the Namibia Institute of Pathology (results not shown).

Seroprevalence estimates and 95% confidence intervals (CI) were calculated using the Wilson-score method for each 5-year age group and for the following sub-groups: gravidity, HIV status, urban/rural residence, facility type (hospital, health center, or clinic), and health district. The odds of seropositivity were calculated by multiple logistic regression while controlling for age group, gravidity, HIV status, urban/rural residence, and facility type. All analyses included sampling weights, which were calculated based on the probability of selection within each of the 12 age–HIV strata and adjusted for non-response (i.e., specimens not available or inadequate for testing) in each of the strata by the propensity cell adjustment method. These weights were then scaled to the total sample size: (weight/sum of weights) × total sample. A large percentage of specimens were not available or suitable for testing. However, demographic information was available for all women sampled, so multiple imputation using chained equations was conducted to impute seropositivity, and the imputed results were compared with estimates based on the subset of non-missing data. As the imputed estimates were not substantially different from the estimates based on the complete non-missing data, only the laboratory results from complete specimens tested are reported. The multiple imputations were done using the mice package in R statistical software version 3.1.2. Other data were analyzed using SAS version 9.3 (SAS Institute, Cary, NC, USA). Comparisons of seroprevalence among groups were done using the Chi-square test on the weighted data. This study received ethical approval from the CDC and the Namibia MoHSS.

3. Results

Based on the sample size calculation, 2692 specimens were selected for inclusion in the study (Table 1); of these, 389 (14%) were not available, 230 (8%) had insufficient volume, 29 (1%) were hemolyzed and therefore could not be used for laboratory testing, and four (0.1%) had a missing test result, resulting in 2040 specimens that were tested and had a laboratory result.

Overall rubella seroprevalence was 85% (95% CI 83–86%) (Table 2). While the 15–19 years age group had the lowest observed seroprevalence (83%) and the 40–44 year old age group had the highest (90%), no statistically significant difference among age groups was seen ($p = 0.208$). Seroprevalence was found to differ by type of facility ($p = 0.033$). Women from urban residences had higher seroprevalence (87%) compared with women from rural residences (83%) ($p < 0.001$).

The multivariable model calculated the odds of rubella seropositivity while adjusting for age group, gravidity, HIV status, urban/rural residence, and facility type (Table 3). Women from urban residences had higher odds of seropositivity as compared with women from rural residences (odds ratio 1.41, 95% CI 1.10–1.82).

Rubella seroprevalence varied by health district and urban/rural residence, from 71% to 100% (Table 4). An analysis comparing demographics of the women whose specimens were not available, of insufficient volume, or hemolyzed, with the characteristics of women whose specimens were tested and included in the analysis, found no substantial differences by age group, gravidity, HIV status, or urban/rural residence (data not shown).

4. Discussion

In 2010, rubella IgG antibody seroprevalence among pregnant women sampled by the National HIV Sentinel Survey in Namibia was 85%. Women residing in urban settings had higher rubella seroprevalence than those in rural settings. Variation was observed in rubella seroprevalence by health district; the lowest point estimate was 71% for women in a rural setting in one health district.

This is the first study of rubella antibody seroprevalence in Namibia. The results are similar to those of previous studies in the African region, which have reported rubella seropositive estimates of 72–99% in women of reproductive age,[7,16–24], and 53–95% in pregnant women.[18,25–41] These serosurvey results and evidence from epidemiological investigations and CRS surveillance indicate that rubella virus is circulating on the African continent, causing rubella infections and CRS.[8,42] For pregnant women, rubella susceptibility is concerning because of the risk of CRS in the fetus.

These findings should be considered in light of limitations. First, only pregnant women 15–44 years old were examined in this study, and the ANC survey was not a random cross-section of the population of pregnant women. Therefore, the results may not be generalizable to all pregnant women in Namibia or to other age groups and populations. When feasible, prospective, population-based surveys could be considered to increase generalizability and allow for the collection of information such as immunization status; however, these studies are time- and resource-intensive, and utilizing specimens already collected and stored might allow for studies that would not otherwise be possible. Second, sample sizes were small at the health district level, limiting conclusions regarding geographic differences. Third, approximately one in four specimens was not available for testing, which might have biased the results. However, it is reassuring that the results from the multiple imputation analysis were very similar to the reported findings.

Currently, inequity in access to rubella vaccine exists, and most countries in Africa do not have RCV available in the public sector. Because of this inequity, regions and countries not using rubella vaccine in the EPI bear the greatest burden of rubella and CRS.[43] Efforts should be made to ensure that resources are available for all countries to introduce RCV into their EPI in accordance with WHO recommendations, including an initial wide age-range nationwide supplemental immunization activity (SIA) and periodic follow-up SIAs to achieve and maintain population immunity to prevent and eventually eliminate rubella and CRS.[44]

When considering the introduction of RCV into the national EPI, a potential concern is a theoretical risk of increasing CRS incidence through a phenomenon termed the ‘paradoxical effect’. This term refers to a hypothetical situation in which persistently low vaccination coverage over time might decrease rubella virus circulation sufficiently, but not eliminate it entirely, shifting both the average age of exposure to rubella virus and rubella susceptibility from children to older age groups, including women of childbearing age, and therefore increasing the incidence of CRS. In such a scenario, however, it is unclear whether the absolute number of CRS cases would actually increase over time compared with the

pre-vaccine era. A shift in susceptibility to older age groups was previously documented in Greece and Costa Rica, but these shifts reflected the implementation of suboptimal strategies. In Greece, rubella vaccine was not introduced into the national EPI and it was available only in the private sector, and an initial wide age-range nationwide SIA was not implemented.[45] In Costa Rica, rubella vaccine introduction was initially limited to 1-year-old children without an initial wide age-range nationwide SIA.[46] Following the implementation of WHO-recommended strategies for RCV introduction, including conducting an initial wide age-range SIA,[47] and as routine RCV vaccination coverage increases in younger age groups, the percentage of rubella cases that occur among older age groups might increase; however, the overall rubella susceptibility in the population, the rubella absolute risk, and the potential risk of CRS will decrease over time.

The disparity in rubella susceptibility among pregnant Namibian women in rural settings compared with urban settings was not unexpected. Consistent with these findings, rubella susceptibility among persons in rural settings was found to be higher than in urban settings during the pre-vaccine era in countries throughout Africa, Europe, the Americas, and Asia.[7,48,49] Moreover, the mean age of infection of reported rubella cases in the pre-vaccine era in Africa was previously found to be significantly higher in rural settings compared to urban settings.[7] This was likely due to longer inter-epidemic periods and the occurrence of rubella infection at older ages in areas with lower population densities and contact rates. When introducing RCV, it is critical to ensure high vaccination coverage in both urban and rural areas to prevent outbreaks. Until all countries have introduced RCV and rubella virus transmission is interrupted, the threat of rubella virus importations, including from bordering countries, will remain a concern, particularly in rural settings.

The Global Measles and Rubella Strategic Plan for 2012–2020 recognizes the need to achieve and maintain high levels of population immunity by providing high vaccination coverage with two doses of measles- and rubella-containing vaccines.[3] Cross-sectional measles and rubella serosurveys provide important evidence to identify immunity gaps in populations and guide vaccination strategies to achieve elimination goals. Serological survey results should be considered along with estimated vaccination coverage and surveillance data to identify susceptible age groups or areas that need to be covered by vaccination activities, decide on vaccine introduction strategies, and determine target age groups and geographic areas for SIAs. In Namibia, based on the results from this study as well as other data sources indicating low measles seropositivity among adults, the MoHSS is considering implementing a nationwide SIA with measles–rubella vaccine among persons aged 9 months to 39 years, a target population of 1.8 million persons.[50] These efforts will be a historic first step on the path to achieve measles and rubella elimination in Namibia, if high coverage with measles–rubella vaccine can be achieved and maintained.

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Table 1

Target and observed sample sizes among pregnant women aged 15–44 years by age group and HIV status, from the 2010 Namibia National HIV Sentinel Survey

Age group, years	HIV status	Total specimens	Target sample size	% of total specimens sampled	Observed sample size	% Not tested (target-observed/target)
15–19	Positive	86	32	37	24	25
	Negative	1264	450	36	335	26
20–24	Positive	282	60	21	46	23
	Negative	1994	422	21	321	24
25–29	Positive	410	110	27	81	26
	Negative	1398	372	27	283	24
30–34	Positive	373	145	39	110	24
	Negative	871	337	39	259	23
35–39	Positive	222	144	65	115	20
	Negative	523	338	65	252	25
40–44	Positive	71	71	100	53	25
	Negative	211	211	100	161	24
All ages	Both	7705	2692	35	2040	24

Table 2

Rubella seroprevalence among pregnant women aged 15–44 years, overall and by age group, facility type, HIV status, gravidity, and setting, from the 2010 Namibia National HIV Sentinel Survey

	Unweighted total, *N*	Weighted percent positive	95% CI[a]	*p*-Value	Weighted percent negative	95% CI[a]	Weighted percent equivocal	95% CI[a]
Overall	2040	85	83–86	-	12	10–14	3	2–4
Age group, years				0.208				
15–19	359	83	79–87		14	10–18	3	2–6
20–24	367	86	83–88		11	9–14	3	2–5
25–29	364	82	78–85		14	11–18	4	2–6
30–34	369	86	82–90		12	9–16	2	0.7–4
35–39	367	88	82–91		8	5–13	4	2–8
40–44	214	90	81–95		7	3–15	4	1–11
Facility				0.033				
Hospital	232	84	79–88		16	12–21	0.4	0.1–2
Health center	301	80	75–84		17	13–21	3	2–6
Clinic	1507	86	84–88		11	9–12	4	3–5
HIV status				0.594				
Positive	429	86	82–89		12	9–16	2	1–4
Negative	1611	85	83–86		12	11–14	3	3–4
Gravidity				0.294				
1	566	84	81–86		13	11–16	4	2–5
2	396	86	83–89		11	9–14	3	2–5
3	349	83	79–87		13	10–17	4	2–6
4+	729	87	84–89		11	8–14	3	2–5
Setting				<0.001				
Rural	1129	83	81–85		14	12–16	4	3–5
Urban	911	87	85–89		10	8–12	3	2–4

CI, confidence interval.

[a]Wilson score.

Table 3

Logistic regression calculating the odds of rubella seropositivity among pregnant women aged 15–44 years, from the 2010 Namibia National HIV Sentinel Survey

	OR	95% CI	*p*-Value
Age group, years			0.318
15–19	Ref.		
20–24	1.16	0.78–1.70	0.467
25–29	0.85	0.54–1.33	0.478
30–34	1.18	0.70–2.36	0.534
35–39	1.27	0.68–2.36	0.453
40–44	1.57	0.64–3.84	0.323
Facility			0.065
Hospital	Ref.		
Health center	0.77	0.49–1.21	0.248
Clinic	1.12	0.77–1.65	0.552
HIV status			0.661
Positive	Ref.		
Negative	0.93	0.67–1.29	0.661
Gravidity			0.446
1	Ref.		
2	1.23	0.85–1.76	0.273
3	0.95	0.62–1.44	0.809
4+	1.20	0.76–1.90	0.433
Setting			0.007
Rural	Ref.		
Urban	1.41	1.10–1.82	0.007

OR, odds ratio; CI, confidence interval.

Table 4

Rubella seroprevalence among pregnant women aged 15–44 years, by health district and urban/rural status, from the 2010 Namibia National HIV Sentinel Survey

District	Setting	Unweighted, n	Weighted % positive	95% CI	Weighted % negative	95% CI	Weighted % equivocal	95% CI
Andara	Rural	53	89	78–95	11	5–23	0	0–7
	Urban[a]	0						
Aranos	Rural	14	100	83–100	0	0–17	0	0–17
	Urban	2	100	36–100	0	0–64	0	0–64
Eenhana	Rural	67	86	76–92	9	4–18	5	2–14
	Urban[a]	0						
Engela	Rural	71	71	60–81	17	10–28	11	6–21
	Urban	1	100	30–100	0	0–70	0	0–70
Gobabis	Rural	11	100	73–100	0	0–27	0	0–27
	Urban	55	93	84–97	7	3–16	0	0–6
Grootfontein	Rural	10	76	47–92	24	8–53	0	0–26
	Urban	40	88	76–95	12	5–25	0	0–8
Oshakati	Rural	41	88	74–95	7	2–19	5	2–17
	Urban	38	72	57–84	20	11–35	8	3–20
Karasburg	Rural	11	77	47–93	10	2–40	12	3–42
	Urban	26	100	87–100	0	0–13	0	0–13
Katutura	Rural[a]	0						
	Urban	76	94	87–98	5	2–13	0.4	0–6
Keetmanshoop	Rural	17	89	65–97	3	0.4–24	8	2–31
	Urban	29	91	75–97	9	3–25	0	0–12
Khorixas	Rural	20	100	83–100	0	0–17	0	0–17
	Urban	21	88	64–97	6	1–29	6	1–29
Katima Mulilo	Rural	26	89	72–96	11	4–28	0	0–13
	Urban	65	89	80–95	10	5–20	0.5	0–6
Lüderitz	Rural	20	84	63–94	8	2–26	9	2–28
	Urban	54	96	87–99	4	1–13	0	0–7
Mariental	Rural	23	87	68–96	13	4–32	0	0–14

District	Setting	Unweighted, n	Weighted % positive	95% CI	Weighted % negative	95% CI	Weighted % equivocal	95% CI
	Urban	18	91	71–98	7	1–26	3	0.3–21
Nankudu	Rural	36	76	61–87	24	13–40	0	0–9
	Urban[a]	0						
Nyangana	Rural	66	86	76–92	14	8–25	0	0–5
	Urban	9	81	50–95	10	2–40	10	2–40
Okahao	Rural	102	79	69–86	19	12–28	3	0.8–8
	Urban[a]	0						
Okahandja	Rural[a]	1						
	Urban	53	85	73–92	10	5–22	5	1–14
Okakarara	Rural	35	81	65–91	19	9–35	0	0–10
	Urban	13	76	49–91	24	9–51	0	0–22
Okongo	Rural	88	86	76–92	7	3–16	7	3–15
	Urban[a]	0						
Omaruru	Rural	29	90	71–97	5	0.8–23	5	0.8–23
	Urban	23	87	69–96	6	1–22	7	2–24
Onandjokwe	Rural	85	79	68–86	21	13–31	0.7	0–6
	Urban[a]	0						
Opuwo	Rural	17	75	49–91	15	4–41	10	2–35
	Urban[a]	0						
Oshikuku	Rural	70	82	71–89	17	10–28	1	0.2–7
	Urban[a]	0						
Otjiwarongo	Rural[a]	0						
	Urban	62	86	75–92	11	5–21	4	1–12
Outjo	Rural	39	77	62–88	21	11–37	1	0.2–11
	Urban	21	73	53–87	3	0.3–19	24	11–45
Outapi	Rural	49	79	66–88	11	5–22	10	5–22
	Urban[a]	1						
Rehoboth	Rural	4	100	52–100	0	0–48	0	0–48
	Urban	22	84	64–94	12	4–31	4	0.7–21
Rundu	Rural	12	87	57–97	5	0.6–33	9	2–37

District	Setting	Unweighted, n	Weighted % positive	95% CI	Weighted % negative	95% CI	Weighted % equivocal	95% CI
Swakopmund	Urban	55	92	82–96	6	2–15	3	0.7–11
	Rural[a]	0						
Tsandi	Urban	56	88	77–94	10	5–20	2	0.4–9
	Rural	87	82	72–89	18	11–28	0.4	0–5
	Urban[a]	0						
Tsumeb	Rural	18	89	67–97	6	1–26	5	0.9–26
Usakos	Urban	54	82	70–90	13	7–24	5	2–14
	Rural	7	100	64–100	0	0–37	0	0–37
Walvis Bay	Urban	15	72	48–87	28	13–52	0	0–18
	Rural[a]	0						
Windhoek Central Hospital	Urban	71	83	72–90	17	10–28	0	0–5
	Rural[a]	0						
	Urban	31	84	68–93	16	7–32	0	0–11

CI, confidence interval.

[a]Number too small to calculate meaningful estimates.