Seroprotection rates of vaccine-preventable diseases among newly arrived Eritrean asylum seekers in Switzerland: a cross-sectional study

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Abstract

Background – According to 2016 WHO/UNICEF country estimates Eritrea has overall high vaccination coverage with immunisation rates for 3 doses of diphtheria/tetanus/pertussis and polio vaccine of 95%, for 2 doses measles vaccine of 85%, and for 3 doses Hepatitis B vaccine of 85%. If confirmed, this could imply that routine basic vaccination of newly arrived Eritreans could be safely omitted.

Methods – We used stored serum samples from two cross-sectional studies that screened newly arrived Eritrean refugees for infectious diseases. Consenting refugees aged 16 years and older who registered in one of three neighbouring cantons in northwestern Switzerland were enrolled between January 2016 and December 2017. Antibody titers against the following vaccine-preventable diseases were measured (applied thresholds for seroprotection in brackets): diphtheria (> 0.1 IU/ml), tetanus (> 0.1 IU/ml), measles (> 150 mIU/ml), rubella (only for women,> 11 IU/ml), varicella (> 50 mIU/ml), hepatitis B (HbsAg Index > 0.9, antiHBc Index > 0.9 and antiHBs > 10 IE/L). Differences between sex and age groups (≤ 25 and >25 years) were measured by Fisher's exact test.

Results – We analysed samples of 133 study participants (20 women, 15%) with a median age of 25 years (range 16-61). Rates of sero-positivity were as follow for women / men respectively: diphtheria 57.9% / 74.8% (difference non significant), tetanus 94.8% / 41.1% ($p<0.001$), measles 73.7% / 76.6% (non sig.), rubella in women 78.9%, varicella 89.5% / 95.3% (non sig.), anti-HBc 15.8% / 26.2% (non sig.), and anti-HBs 15.8% / 17.8% (non sig.)

Conclusion – Sero-prevalence for vaccine-preventable infections did not meet levels required to confer herd-immunity in any of the human-to-human transmissible diseases that were studied. In general, the strategy proposed by the Federal Office of Public Health to offer basic immunization to all newly arrived refugees, including newly arriving Eritrean refugees, is justified.

Key words

Eritrea; asylum seekers; vaccine-preventable diseases; migrants; herd immunity; vaccination coverage

Background

In 2015 and 2016, humanitarian crises in the Middle and Far East as well as in the horn of Africa lead to a large wave of migrants seeking asylum in Europe. In most countries of origin, the public health system had seriously deteriorated, if not completely collapsed. Hence, vaccination coverage was expected to be markedly lower than in previous periods. In refugee camps the en route provision of primary health care, including immunization, relied heavily on the presence of non-governmental organisations and was impeded. Studies in newly arrived asylum seekers in Germany[1-3] showed seropositivity rates of various vaccine-preventable diseases (VPD) well below those known to confer herd immunity.

Hence, many countries receiving refugees issued blanket recommendations to offer primary immunization[4-7] to newly arriving refugees, irrespective of age. In Switzerland, all newly arrived asylum seekers are informed on access to screening for infectious diseases and are offered care and vaccination in federal registration centres (FRC). Recommendations to provide age-specific basic immunization to children and catch-up immunization to adults exist.[8] However, vaccination was explicitly delegated to primary health care physicians at the community level once the formal process of registration was finalized, i.e. often after several months. Adherence to this recommendation is not known, but likely to be low. Due to repeated outbreaks of varicella and cases of cutaneous diphtheria in asylum seekers, from 2018 onward, the recommendation has changed to start a full course of age-specific basic immunization early after arrival at the FRC level.

Eritreans account for the largest group of asylum seekers in Switzerland[9] (18.7% of all newly registered asylum seekers in 2017). The Expanded Program of Immunization (EPI) in Eritrea was launched in 1980, initially including vaccines against diphtheria, pertussis, tetanus, poliomyelitis, measles and tuberculosis. However, noticeable progress in program implementation was only seen after independence in 1991. Hepatitis B was introduced in

2002 and the pentavalent vaccine combining the vaccines against diphtheria, pertussis, tetanus, hepatitis B and *Haemophilus influenzae* type b was introduced in 2008. According to data from the World Health Organisation and UNICEF (WHO/UNICEF), Eritrea is among one of the countries with very high vaccine coverage rates.[10] With reference to 2016 WHO/UNICEF data, Eritrea had a 95% coverage for the completion of three doses of diphtheria/tetanus/pertussis and polio (DTP3 and Pol3), 93% for at least one dose of a measles containing vaccine and 95% for the 3rd dose of hepatitis B containing vaccine following the birth dose. Data from an EPI coverage survey in the year 2000 among children 0-23 months showed only marginally lower coverage rates: DPT3/OPV3 coverage was 93.6%, and measles coverage (one dose) was 82.5%. These are very high coverage rates, higher than in some European countries. Consequently, young Eritrean asylum seekers may not need to be fully re-immunised upon arrival in Europe. This would save unnecessary vaccine doses at the individual as well as at public health levels. Our objective was to assess the percentage of newly arrived Eritrean asylum seekers with protective antibody titers for six VPDs. Studies on VPDs among newly arrived asylum seekers in other European countries included mainly participants from the WHO Eastern Mediterranean Region (EMRO), namely from Syria, Iran, Iraq and Afghanistan, and only few Eritreans were included. To our knowledge, this is the largest sample assessing immune responses against multiple VPDs in Eritreans.

Methods

We used stored serum samples from two cross-sectional studies that screened newly arrived (<12 months since entry) Eritrean asylum seekers for infectious diseases. Both studies were conducted in three neighbouring cantons in northwestern Switzerland. Recruitment and sampling methods have been published previously.[11,12] Samples were obtained between January 11th 2016 and December 27th 2017. Ethics approval was granted from the regional ethics committee (EKNZ 2015-353/PB_2017-00092 Amendment 3 & 4 and EKNZ 2016-

119 00005). We enrolled consenting refugees aged ≥16 years (Cantons Basel-Stadt and -Land) or
120 aged ≥15 (Canton Solothurn). We did not ask for vaccination history, as we could not verify
121 this information as it is highly unlikely for this population to arrive with a vaccination card.
122 Antibody titers against the following VPD were measured (applied thresholds for sero-
123 protection in brackets): diphtheria (> 0.1 IU/ml), tetanus (> 0.1 IU/ml), measles (> 150
124 mIU/ml), rubella (only for women, > 11 IU/ml), varicella (> 50 mIU/ml), hepatitis B (HBsAg
125 Index > 0.9, anti-HBc Index > 0.9 and anti-HBs > 10 IE/L).

126 Sample preparation and analysis
127 Blood samples were collected in serum tubes and centrifuged at 2000g for 5 min after
128 complete coagulation at room temperature. After separation, the serum was frozen in aliquots
129 at minus 20°C until performance of serological tests. Rubella virus IgG and hepatitis B virus
130 (HBs Antigen qualitative, anti-HBc total Ig, anti-HBs IgG were analysed on an Architect®
131 system (Abbott, Chicago, USA), a fully automated immune-analyser based on
132 chemiluminescent microparticle immunoassays (CMIAs). IgG antibodies against measles and
133 varicella virus were determined using Serion ELISA classic measles Virus IgG kit and
134 varicella zoster virus IgG, respectively (Virion/Serion GmbH, Würzburg, Germany)
135 according to the manufacturer's instruction. IgG diphtheria and IgG tetanus antibodies were
136 detected by VaccZyme diphtheria toxoid IgG ELISA and VaccZyme tetanus toxoid IgG
137 ELISA from Binding site (Birmingham, UK).

138 Results are presented as median titers and interquartile ranges (IQR), and percentage of the
139 participants with a titer above the indicated threshold for sero-protection. Fisher's exact test
140 was used to detect differences between sex and age groups (≤ 25 and > 25 years of age).
141 These two age groups correspond to about half of the participant population but they also
142 represent those born before and after 1991, the year of Eritrean independence and when EPI
143 implementation started to progress.

All serological analyses were performed at the Institute for Infectious Diseases, University of Bern.

Results

We included 133 Eritrean asylum seekers with a median age of 25 years (range 16-61), 47.4% were ≤ 25 years old, and 98.5% were below the age of 45 years. Women made up 15% (n=20) of all participants.

The distribution of disease-specific sero-prevalence is presented in table 1, table 2 and figure 1. There was no difference in sero-protection rates between the sexes except for tetanus, where 18 (95%) out of 19 women had a positive titer compared to 44 (41%) out of 107 men ($p<0.001$). In the age group above 25 years, 36% had positive antibodies against the Hepatitis B core antigen (anti-HBc) compared to 11% in those younger than 25 years ($p=0.001$). Similarly, in the older age group 23% had antibodies against Hepatitis B surface antigen (anti-HBs) compared to 11% in the younger group (trend, $p= 0.097$). In the whole population 69.9% remained susceptible for Hepatitis B infection and would qualify for vaccination. For the other diseases, there was no difference between the two age groups, though point estimates indicated a trend towards higher sero-prevalence in those older than 25 years (data not shown).

Discussion

In newly arrived Eritrean asylum seekers, we found overall lower rates of sero-positivity for VPDs than anticipated - given the WHO/UNICEF immunization coverage figures for Eritrea in 2016.[10] Sero-prevalence in this population failed to reach the threshold expected to confer herd immunity against measles and rubella (≥ 95%[13]) and against diphtheria and varicella (80% and 91% respectively[14]). The implications are that this population remains vulnerable to primary infection with these diseases after arrival in Switzerland.

Our study shows lower rates of sero-positivity for measles, rubella, and varicella than other European studies among newly arrived asylum seekers in the same period. A study from Germany reported an overall IgG sero-positivity of 88.5% for measles, 77.9% for rubella and 95.9% for varicella.[2] However, the majority of participants in that study (83%) were from the WHO Eastern Mediterranean Region (EMRO) and only 4.6% from African regions. Another study in the Netherlands showed a relatively high overall sero-protection rate in 622 participants: 88% for measles, 94% for rubella and 96% for varicella.[3] Again, most study participants were from EMRO, and only 9% (n=56) were from Eritrea. An Italian study[15], including 134 Eritreans, found 79.9% positive measles antibodies in this population, this is closer to the rate reported in our study (76.2%).

Furthermore, regarding diphtheria and tetanus, the latter study found high overall sero-protection rates of 82% and 98% respectively.[3] Eritreans, however, were the exception, with a markedly lower tetanus sero-prevalence of 41%. Another study conducted in Germany[1] (without mention of country of origin of asylum seekers) found similarly low levels of sero-protection, stating that only 43.7% and 23.9% had sufficient tetanus respectively diphtheria IgG levels that corresponded to long-term protection. Our study corresponds to these results: only 68.4% of both sexes showed to have a positive titer for diphtheria and only 41.1% of men had a positive titer for tetanus. However, women showed a surprisingly high percentage with positive tetanus titers (95%), most probably indicating that they had received booster doses in pregnancies (as recommended by the WHO).

Nearly one quarter of the study participants showed positive Hepatitis B core antibodies (anti-HBc), as a marker of past or current infection with Hepatitis B. However, only 1.5% had a positive HBs-antigen, indicative of chronic infection. This implies that most participants had experienced functional cure with loss of HBs-antigen. This result goes in line with data from general estimates for Eritrea[16], which classify it as one of only three countries in the African

193 region with a prevalence of positive HBs-antigen of < 5%. Immunity to Hepatitis B, as
194 measured by positive Hepatitis B surface antibodies (anti-HBs), was only found in 16.5% of
195 the participants.

196 One of the strengths of this study is that it provides data for the largest asylum seeker
197 population in Switzerland, for whom so far data has been lacking. Furthermore, age
198 distribution of the study population is similar to the data provided by the federal asylum
199 seekers statistics,[9] allowing us to assume that our data are representative for the population of
200 Eritrean asylum seekers.

201 The limitations of our study lie in the moderate sample size and the low number of female
202 participants (15%). In addition, only humoral antibody response was measured, and follow-up
203 antibody titers in response to booster doses to assess cellular memory function was not
204 measured. Hence, boostable cellular immunity to these diseases may be underestimated.

205 In summary, we found insufficient levels of sero-protection for all measured VPDs in this
206 population, leaving them vulnerable to primary infection within Switzerland. The
207 recommendation to offer basic immunization to all newly arrived asylum seekers in
208 Switzerland appears justified, also for persons originating from Eritrea.

Conflict of interest

The authors have declared no conflict of interest.

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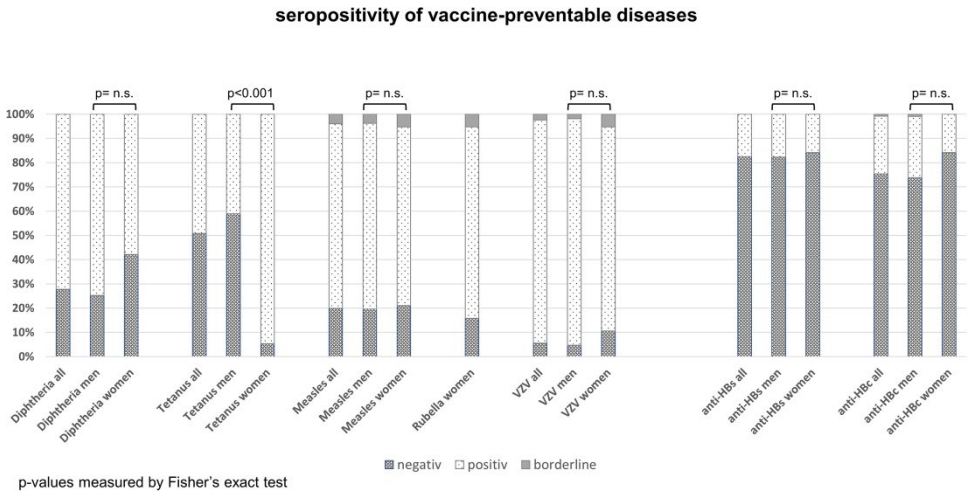

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270 **Table 1 – Serology results of Diphtheria, Tetanus, Measles, Rubella and Varicella**

	reference		median titer (IQR)	positive* % (n)	weakly positive % (n)	borderline % (n)	negative % (n)	missing % (n)[&]	p-value[%] men vs. women
Diphtheria IgG [IU/ml]	positive >0.1	**all**	**0.17 (0.10 – 0.44)**	**68.4% (91)**	na	na	**26.3 % (35)**	5.3% (7)	
		women		57.9% (11)			42.1 % (8)		0.17
		men		74.8% (80)			25.2 % (27)		
Tetanus IgG [IU/ml]	positive >0.1	**all**	**0.09 (0.07 – 0.48)**	**46.6% (62)**	na	na	**48.1 % (64)**	5.3% (7)	
		women		94.8% (18)			5.3% (1)		<0.001
		men		41.1% (44)			58.9 % (63)		
Measles IgG [mIU/ml]	negative <150 borderline ≥150-200 positive >200	**all**	**639 (205 – 1465**	**76.2% (96)**	na	**4.0% (5)**	**19.8 % (25)**	5.3% (7)	

			)						
		wom en		73.7% (14)		5.3% (1)	21.0 % (4)		
		men		76.6% (82)		3.7% (4)	19.6 % (21)		0.8
Measles IgG [mIU/ml], if borderline to positive	negative <150 positive ≥150	**all**	**639 (205 – 1465)**	**75.9% (101)**	na	na	**18.8 % (25)**	5.3% (7)	
		wom en		78.9% (15)			21.0 % (4)		1.0
		men		80.4% (86)			19.6 % (21)		
Rubella IgG [IU/ml], *only women, n=20 (15%)*	negative <5 borderline ≥5-10 positive >10	wom en	**29.8 (21.6 – 73.3)**	**78.9% (15)**	na	**5.3% (1)**	**15.8 % (3)**	5% (1)	n.a.
VZV IgG [mIU/ml]	negative <50 weakly positive ≥50-100 positive >100	**all**	**473 (222 – 849)**	**87.2% (116)**	**2.3% (3)**	na	**5.3% (7)**	5.3% (7)	
		wom en		84.2% (16)	5.3% (1)		10.5 % (2)		0.19
		men		93.5%	1.9%		4.7%		

				(100)	(2)		(5)		
VZV IgG [mIU/ml], if weakly positive to pos.	negative <50 positive ≥50	**all** women men	**473 (222 – 849)**	**89.5% (119)** 89.5% (17) 95.3% (102)	na	na	**5.3% (7)** 10.5 % (2) 4.7% (5)	5.3% (7)	0.28

Abbreviations and footnotes: VZV – Varicella-Zoster virus; IU/ml – international units / millilitre; * positive indicates the percentage of participants with a titer that confers protection; [&] missing are always data from the same 6 men and 1 woman; [%] Fisher's exact test

Table 2 – Hepatitis B status among Eritrean asylum seekers

	All*[&], in %
Susceptible	69.9%
Chronic Hepatitis B	1.5%
Immunity from previous infection	21.8%
Immunity from vaccination	0.8%

*p-value for difference between sexes (Fisher's exact) for all analyses >0.5

[&] missing values: 7

Definitions

- Susceptible: HBs-antigen negative | anti-HBc and anti-HBs negative
- Chronic Hepatitis B: HBs-antigen positive | anti-HBc and anti-HBs negative
- Immunity from previous infection: HBs-antigen negative | anti-HBc positive +/- anti-HBs
- Immunity from vaccination: HBs-antigen and anti-HBc negative | anti-HBs positive