

Research Article

Impact of Sex, Age and Body Habitus on RBD-specific Antibody Response After Two Doses of Sinopharm BBIBP-CorV Vaccine

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Abstract

Background: Mongolia started its nationwide vaccination campaign against COVID-19 on 23 February 2021 after receiving the first batch of the inactivated BBIBP-CorV. Age and body habitus of vaccinees may be associated with the immune effector functions. Several systematic reviews and meta-analyses suggested lower immunogenicity of vaccines against SARS-CoV-2 infection in the older adult population and obese individuals. We aimed to establish a possible relationship between post-vaccine seroconversion rate and some biometric characteristics in the Mongolian cohort of vaccinees after two shots of the Sinopharm BBIBP-CorV vaccine.

Materials and Methods: We collected serum samples from 846 eligible vaccinees before the first dose of the BBIBP-CorV vaccine and 21-28 days after the second dose of the same vaccine. Anti-SARS-CoV-2 Receptor Binding Domain (RBD) Immunoglobulin class G (IgG) and M (IgM) titer were measured in all samples.

Results: 686 (81.1%) of 846 vaccinees received the Sinopharm BBIBP-CorV vaccine demonstrated seroconversion. Vaccinees with seroconversion had a younger mean age and lower mean body-mass index (BMI) than non-responders. Seroconversion rate according to age of vaccinees tends to decrease and obese vaccinees demonstrated a greater portion among non-responders. The Optimal Cut-Point (OCP) of age for seroconversion was found to differ significantly in male and female vaccinees. BMI has shown prediction ability for seroconversion only in male vaccinees but not in females. Using Receiver Operating Characteristics (ROC) analysis, we found 39 years for males and 41 years for females as a crucial milestone increasing the probability of seronegativity 2.5 times on average. A BMI higher than 29.1kg/m² in male vaccinees was considered an acceptable predictor for seroconversion increasing the probability of seronegativity 2.4 times on average.

Conclusion: The above findings allow us to summarize the sex-adjusted approach to biometric characteristics has an improved predictiveness for post-vaccine antibody response.

Keywords: COVID-19; Sinopharm BBIBP; Seroconversion; Body Habitus; Sex-Adjustment

Introduction

Mongolia started its nationwide vaccination campaign against COVID-19 on 23 February 2021 after receiving the first batch of the inactivated BBIBP-CorV vaccine from Sinopharm, China. Priority for the vaccination with this vaccine was given to high-risk healthcare workers and government employees working in frontline places. With the gradual coverage of this group, vaccination of the general adult population began at the end of March 2021 [1].

Individual biometric parameters may be associated with the immune effector functions such as immunocompetent cell activation and production of antigen-specific antibodies to vaccine stimuli [2]. Declining immune function with age substantially contributes to the decreased efficacy of vaccines in elderly persons. The underlying complex changes in the immune system are collectively termed immunosenescence and they affect cell types of both the innate and the adaptive immune system [3]. The immune function of the elderly is weakened and most of them are complicated by chronic underlying diseases. Several systematic reviews and meta-analyses suggested lower immunogenicity of vaccines against SARS-CoV-2 infection in the older adult population [4,5].

Obesity is associated with immune cell-mediated inflammation [2,6]. The current research reports focused on the impact of obesity on vaccination for SARS-CoV-2 are contradictory and numerous questions remain unanswered [7]. In this study, we aimed to establish a possible relationship between post-vaccine seroconversion rate and some biometric characteristics in the antibody-naïve Mongolian cohort of vaccinees after two shots of the Sinopharm BBIBP-CorV vaccine.

Material and Methods

Study Design and Population

We used a prospective cohort study design and enrolled 846 eligible vaccinees who received two doses of the Sinopharm BBIBP-CorV vaccine from April-May to July-August of 2021. The sociodemographic and biometric characteristics of vaccinees are shown in Table 1.

	Males, n = 302 (35.7%)	Females, n = 544 (64.3%)	Total, n = 846 (100.0%)
Age (years)			
Mean (M $\pm$ SD)	37.1 $\pm$ 11.8	41.5 $\pm$ 13.3	39.9 $\pm$ 12.9
Median (IQR)	35.0 (15)	40.0 (20)	38.0
CI95	35.2-38.5	40.3-43.1	38.8-41.0
Variation	18-77	18-93	18-93
Population groups, count (percent in sex group)			
Frontline employees†	194 (64.2)	411 (75.6)	605 (71.5)
Vaccinees with increased risk‡	10 (3.3)	33 (6.1)	43 (5.1)
General adult population¶	98 (32.5)	100 (18.4)	198 (23.4)
Body habitus, count (percent in sex group)			
Underweight (BMI: < 18.5 kg/m ²)	1 (0.6)	6 (1.5)	7 (1.2)
Normal weight (BMI: 18.5-24.9 kg/m ²)	36 (22.4)	152 (37.5)	188 (33.2)
Overweight (BMI: 25.0-29.9 kg/m ²)	77 (47.8)	153 (37.8)	230 (40.6)
Obesity (BMI: $\geq$ 30.0 kg/m ²)	47 (29.2)	94 (23.2)	141 (24.9)
Subtotal#	161 (28.4)	405 (71.6)	566 (100.0)
BMI (kg/m ²)			
Mean (M $\pm$ SD)	28.0 $\pm$ 5.0	26.7 $\pm$ 5.2	27.1 $\pm$ 5.1
Median (IQR)	27.7 (5.0)	26.0 (6.6)	26.6
CI95	27.2-28.8	26.2-27.2	26.7-27.5
Variation	18.4-60.2	17.3-68.7	17.3-68.7

Note: M, mean; SD, standard deviation; IQR, interquartile range; †-healthcare workers and government employees worked in the frontline of pandemics; ‡-vaccinees with increased risk developing severe COVID-19 included patients received immunosuppressive therapy for the last 6 months due to autoimmune or systemic inflammatory diseases and elderlies aged $\geq$ 60 years; ¶-general population aged 18-59 years not belonging to the first two groups; #-BMI was available in 566 vaccinees only

Table 1: Sociodemographic and biometric characteristics of vaccinees who received two doses of Sinopharm BBIBP-CorV.

We collected personal information, biometric data and serum samples of vaccinees before the first dose and 21-28 days after the second dose of vaccine.

Vaccine

All study participants received Sinopharm (BBIBP-CorV) manufactured at the Beijing Institute of Biological Products (Sinopharm), People's Republic of China. The dose administered 0.5 mL, interval between shots 4-10 weeks.

Seroprevalence

We collected serum samples before the first dose of the vaccine and 21-28 days after the second dose. Anti-SARS-CoV-2 Receptor Binding Domain (RBD) Immunoglobulin class G (IgG) and M (IgM) titer were collected serum samples using Enzyme-linked immune sorbent assay (ELISA, Proteintech®, USA). We collected serum samples before the first dose of the vaccine and 21-28 days after the second dose. Anti-SARS-CoV-2 Receptor Binding Domain (RBD) Immunoglobulin class G (IgG) and M (IgM) titer were measured in all collected serum samples using Enzyme-linked immune sorbent assay (ELISA, Proteintech®, USA). If the titer of both RBD-IgG and RBD-IgM, either one of these antibodies showed a value of higher than 6.25ng/mL, a sample was considered previous or ongoing infection and excluded from further study [8].

Statistical Analysis

We performed statistical analysis using descriptive and inferential methods. The distribution of seroprevalence among population subgroups was compared using Pearson's Chi-square test. Continuous variables such as age, BMI and antibody titer in population groups were compared using an Analysis of Variance test (ANOVA). The predictiveness of biometric data was evaluated using ROC analysis. The risk of biometric variables for seronegative state after two-dose vaccination was calculated using Risk Ratio (RR) in a contingency table. Statistical significance was expressed using p-values of < 0.05, < 0.01, < 0.005 and < 0.001.

Results

Seroconversion and Protective Antibody Titer in Population Groups

A total of 686 (81.1%) of vaccinees received the Sinopharm BBIBP-CorV vaccine demonstrated seroconversion (responders), showing a four-fold increased anti-SARS-CoV-2 RBD-IgG titer and in 160 (18.9%) vaccinees we did not detect sufficient titer of protective antibodies (non-responders). No significant difference was found in seroconversion rates in male and female vaccinees (81.5% and 80.9%, respectively, $p > 0.05$). The seroconversion rate in priority population groups varied significantly (87.1% for frontline employees, 62.8% for a population with increased risk for developing severe disease and 66.7% for the general adult population; $p < 0.001$). The average titer of anti-SARS-CoV-2 RBD-IgG antibody in responders after 21-28 days of the second dose of vaccine was 45.5 ± 50.8 ng/mL (CI95: 41.7-49.4 ng/mL; variance: 6.7-329.6 ng/mL; median 28.0 ng/mL). No significant difference was found in mean titer in male and female vaccinees (47.6 ± 54.0 and 44.4 ± 49.0 ng/mL, respectively, $p > 0.05$).

Relationship Between Postvaccine Antibody Response and Biometric Characteristics of Vaccinees

Sex and age. Vaccinees with antibody response had a younger mean age compared to non-responders (38.7 ± 12.1 vs 45.3 ± 14.9 years, $p < 0.001$; respectively).

We calculated the sex-adjusted Optimal Cut-Point (OCP) for age stratified by the seroconversion rate using ROC analysis (Fig. 1).

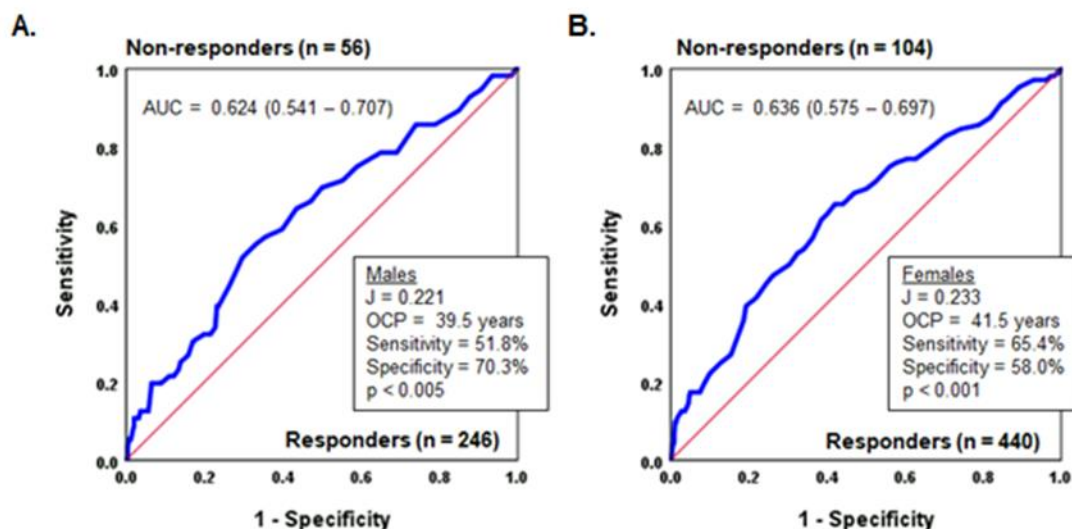


Figure 1: ROC curve of age of vaccinees stratified by the seroconversion rate. A: Male vaccinees; B: Female vaccinees; AUC, area under the curve; J, Youden index; OCP, optimal cut-point of age; p, asymptotic significance (two-sided).

Furthermore, using the calculated age OCPs, we established sex-adjusted and age-dependent probability (OD) and Relative Risk (RR) for no response after the two shots of the BBIBP-CorV vaccine (Table 2).

		RBD-specific antibody response		Total
		Response	No-response	
Sex-adjusted age	Males $\leq$ 39 years and females $\leq$ 41 years	428 (87.2)	63 (12.8)	491 (100.0)
	Males $>$ 39 years and females $>$ 41 years	258 (72.7)	97 (27.3)	355 (100.0)
Total		686 (81.1)	160 (18.9)	846 (100.0)
OD = 2.5 (1.8-3.6); RR = 1.2 (1.1-1.3); p < 0.001				
OD: Odd Ratio; RR: Relative Risk				

Table 2: Sex-adjusted age-dependent probability and relative risk for seroconversion, n (%).

When comparing population groups, we found significantly increased sex-adjusted OD and RR for no response in older people of frontline workers (OD = 2.7; RR = 1.1; p < 0.001) and the general adult population (OD = 2.7; RR = 1.4; p < 0.005). However, the group of vaccinees with increased risk for developing a severe disease has shown no significant risk (p < 0.05), probably, due to a small number of observations.

BMI. Vaccinees who demonstrated RBD-specific antibody response had lower mean BMI compared to non-responders (26.8 $\pm$ 4.9 vs 28.6 $\pm$ 6.0 kg/m², p < 0.005; respectively). The percentage of responders among obese vaccinees (105 out of 138 or 76.1%) was much compared to normal-weight (159 out of 186 or 85.5%, OD = 1.8; p < 0.05) and overweight (195 out of 224 or 87.1%, OD = 2.1; p < 0.05) vaccinees. ROC analysis demonstrated the significant impact of BMI on antibody response state only in male vaccinees (Fig. 2).

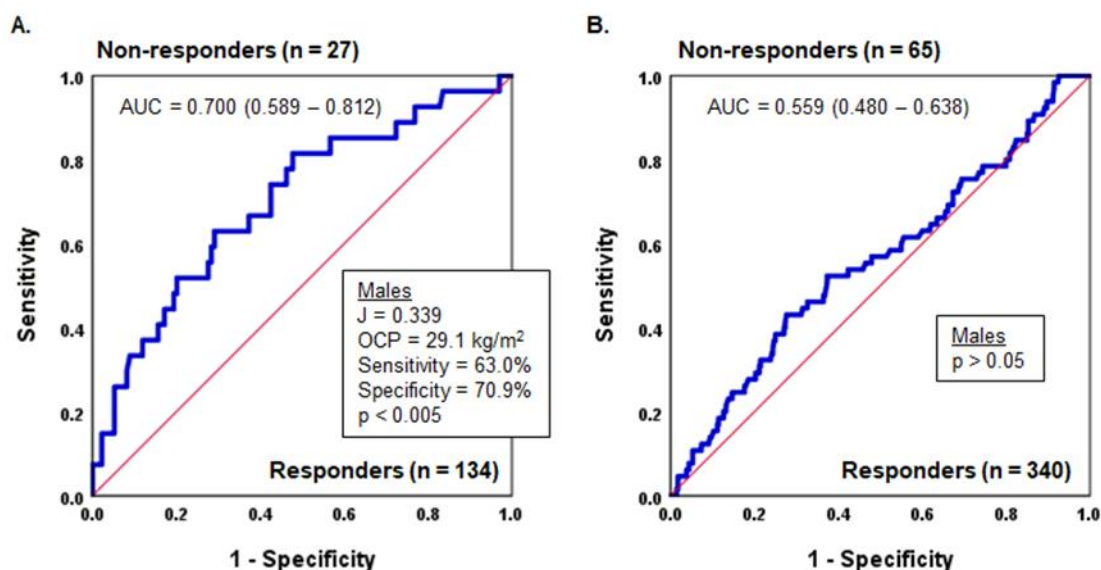


Figure 2: ROC curve of BMI of vaccinees stratified by the seroconversion rate. A: Male vaccinees; B: Female vaccinees; AUC, area under the curve; J, Youden index; OCP, optimal cut-point of age; p, asymptotic significance (two-sided).

Males who show a BMI above 29.1 kg/m² have demonstrated a significantly increased probability and relative risk of producing no SARS-CoV-2 RBD-specific IgG compared to females and males with a BMI less than the OCP (Table 3).

		RBD-specific antibody response		Total
		Response	No-response	
BMI	Males ≤ 29.1 kg/m ² and females	433 (85.2)	75 (14.8)	508 (100.0)
	Males > 29.1 kg/m ²	41 (70.7)	17 (29.3)	58 (100.0)
Total		474 (83.7)	92 (16.3)	566 (100.0)
OD = 2.4 (1.3-4.4); RR = 1.2 (1.0-1.4); p < 0.01				
OD: Odd Ratio; RR: Relative Risk				

Table 3: Sex-adjusted body habitus dependent probability and relative risk for seroconversion, n (%).

Discussion

We established an immunogenicity rate of 81.1% for the Sinopharm BBIBP-CorV vaccine. Globally, the antibody production rate of this vaccine is well-documented and showed a seroconversion rate of 60.6-99.2% [9-19].

We found a gradual decrease in the count of seropositive individuals by age in our cohort and we suggested 39 years for males and 41 years for females as a crucial milestone increasing the probability of a non-response state after two-dose BBIBP-CorV vaccine 2.5 times on average. A higher seroconversion rate in younger vaccinees compared to older counterparts immunized by the inactivated vaccine against COVID-19 has been reported in several cohorts [18,20,21]. However, fewer studies have reported the correlation between seroconversion with gender and age is not significant [19]. We found declining immune function with age substantially contributes to the decreased efficacy of vaccines in elderly persons. The underlying complex changes in the immune system are collectively termed immunosenescence and they affect cell types of both the innate and the adaptive immune system [3,22,23].

Conclusion

In this study, the seroconversion in male vaccinees varied according to their body habitus. We found a lower percentage of antibody response among obese vaccinees (76.1%) compared to normal-weight (85.5%) and overweight (87.1%) vaccinees. In particular, a BMI higher than 29.1 kg/m² in male vaccinees was considered an acceptable predictor for seroconversion increasing

seronegativity 1.3 times on average. Reduced seropositivity rate among individuals with obesity/overweight compared to normal-weight individuals was reported by many authors. The above findings allow us to summarize the sex-adjusted approach to biometric characteristics has an improved predictiveness for post-vaccine antibody response.

Conflict of Interest

The author declares no conflicts of interest.

Acknowledgment

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