

Pre-Vaccination Profiles and Factors Associated with Suspected COVID-19 Infection in Vaccine Candidates in The Democratic Republic of Congo: A Cross-Sectional Study

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ABSTRACT

Background: The aim of this study was a pre-vaccination profile assessment to identify risks for adverse events.

Methods: Cross-sectional, analytical study including 1,500 individuals presenting for COVID-19 vaccination at the Cliniques Universitaires de Kinshasa between April 19 and December 31, 2021.

Results: Of 1500 individuals examined, 69.3% were male (sex ratio 3H/1F), mean age 47.5±16.0 years. A significant inverse relationship was observed between age and AST on the one hand ($p=0.015$); and age and ALT on the other ($p=0.011$). The correlation was 46.3% for AST and 46.9% for ALT. A total of 9.5% of individuals presenting for vaccination had an NLR greater than or equal to 2, signifying a COVID-19 infection. Female gender (aOR: 2.94 IC95%: 1.99-3.96), the presence of comorbidity (aOR: 2.83; 95%CI: 1.88-3.88), the presence of abnormal PAL (aOR: 2.12; 95%CI: 1.24-3.62) and the presence of abnormal RBC (aOR: 1.92; 95%CI: 1.22-3.01) were the factors independently associated with the COVID-19 infection in the study population.

Conclusion: The results show a normal biological profile, but they highlight the importance of certain simple biological markers in screening for COVID-19 infection in an asymptomatic population.

Keywords: Profile, COVID-19 vaccine, cross-sectional study, NLR ratio, pre-vaccination screening, DRC

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INTRODUCTION

It is well known that corona virus 19 (COVID-19) disease causes significant morbidity and mortality in most communities. [1,2] The literature describes that the risk of contracting COVID-19 is associated with different levels of exposure. The population living in the community is considered to be the main group at risk. [3] In the third year of the global COVID-19 pandemic, public health actors continued to focus on reducing the risks of the pandemic through the distribution of COVID-19 vaccine [4,5] as part of integrated governmental and community-wide approaches [6,7].

In line with this approach, the government of the Democratic Republic of Congo (DRC) acquired the right to vaccinate the population against COVID-19 to reduce this global pandemic. The COVID-19 vaccines deployed in the DRC composed of moderna, AstraZeneca and Pfizer vaccine, like many vaccines for other diseases, were administered intramuscularly to optimize immunogenicity, minimizing post-immunization adverse events (MAPI). [8] These MAPIs can be linked to several factors among others the disruption of individuals' epidemiological or biological profile. Data from the literature have shown that the SARS-CoV-2 spike interacts with several systems in particular the renin-angiotensin system (via its binding to ACE2) and will deregulate it by anticipating the pathogenicity of the virus and vaccines. [9] The spike in biodistribution of lipid nanoparticles (LNPs) in liver, spleen, ovaries and testes, bone marrow, can turn into a prion in the presence of a disturbance in the biological profile of individuals receiving the COVID-19 vaccine. [10] Thus, knowledge of the biological profile of individuals expected to receive the COVID-19 vaccine is paramount in order to avoid cross-reactions and adverse post-immunization events.

In the DRC, studies on the epidemiological and biological profile of individuals prior to vaccination against COVID-19 should be initiated to exclude people with biological disturbances, in order to avoid MAPI and prevent it from having a fatal outcome. Indeed, in a context where full vaccination against COVID-19 was less than 5% in some provinces such as North Kivu in February 2023, compared to only 10% in Kinshasa and more than 50% in East Kasai, the use of prior biological profiling becomes crucial. This approach would make it possible to effectively target at-risk individuals, optimize the use of limited resources, reassure the population, and overcome barriers such as vaccine hesitancy, which is largely fueled by misinformation and a lack of trust in the authorities. Some hypotheses were put forward to see if certain demographic and biological factors are associated with markers of prior COVID-19 infection. This study was carried out a pre-vaccination profile assessment to identify risks for adverse events.

MATERIALS AND METHODS

Study design and population: This was a cross-sectional,

analytical study, which was conducted at the Cliniques Universitaires de Kinshasa of the Faculty of Medicine of the University of Kinshasa in the Democratic Republic of Congo between April 19 and December, 31, 2021 which coincided with the introduction of COVID-19 vaccination in the DRC. The study was conducted in accordance to relevant guidelines and regulations. The study was reviewed and approved by the National Health Ethics Committee at No. 201/CNES/BN/PMMF/2021 from March 28th, 2021. Written informed consent was obtained from all the participants and/or their legally acceptable representatives. The study population consisted of people who came voluntarily to be vaccinated against SARS-COV-2. Sampling was exhaustive and based on convenience. The sample size was 1500 participants who had verbally agreed to take part in the study. Inclusion criteria were the status of the asymptomatic person having accepted a blood sample before receiving one of the 3 vaccines available for vaccination (AstraZeneca, Moderna and Pfizer), residing in Kinshasa and age greater than or equal to 18 years. The non-inclusion criterion included individuals under 18 years of age, patients with COVID-19 hospitalized in COVID-19 treatment centers and those who did not agree to participate in the study.

Given the method used to vaccinate adults and adolescents, unlike routine vaccination which only takes children into account, the sample size estimates for this study will not use vaccination data from other sub-Saharan countries. Instead, key indicator values are assumed to be 50% in order to maximize the sample size estimate. A precision of 10 percentage points in a survey cycle corresponds to the ability to detect a minimum change of 20 percentage points over time. This is important given that one of the objectives of the study is to serve as a baseline for evaluating any future interventions in the vaccination sector in the DRC. The following formula and assumptions were used to estimate the number of individuals required:

$$n = \text{deff} \times \frac{[Z_{1-\alpha}^2 \times P(1-P)]}{d^2} \times \text{CPF}$$

Where, n = desired sample size (by urban/rural area and type of point of sale) ; P = assumption regarding the proportion of the population, equal to 0.5 ; $Z_{1-\alpha}$ = normal value of the standard deviation $1-\alpha$ corresponding to an error α (type I) with a two-tailed test, equal to 1.96 ; d = the desired absolute precision for the estimate / half the width of the desired confidence interval, equal to 0.1 ; deff = the sampling effect in the case of sampling for public health purposes, equal to 2 ; CPF = the finite population correction, a correction applied to the sample size calculation when the population size is known (or assumed to be less than a given value) and the sample represents more than 5% of the population. This calculation resulted in a minimum sample size of 540 individuals for this study to be conducted.

Data collection and haematological and biochemical analyses: Data were collected using a pre-established

form. Parameters of interest were selected and collected by means of questioning for gender, age, occupation and presence of comorbidity were collected through self-reporting by individuals; by blood sampling to carry out paraclinical examinations (haematology and biochemistry).

Biological data included blood data. A 5-ml venous blood sample was taken from the elbow crease on dry tubes and EDTA tubes for the various analyses, on arrival of the candidate for vaccination against COVID-19.

Samples were first packed in absorbent paper, then in an appropriate Biohazard Bag transport specimen bag, and then in an isothermal container with cold accumulators. All samples were stored in a blood bank refrigerator, brand XY130 (China) at -20 to -80°C at the Laboratoire Central des Cliniques Universitaires de Kinshasa until the day of analysis. Blood samples collected at both times were processed within 24 hours of collection for haematological analysis and later for biochemical analysis. Tubes for biochemical analysis were run on a spectrophotometer branded RAYTO 9200 Semi-auto chemistry Analyzer, SN: 602321157 IE (Rayto, Guangming, China). Results were interpreted according to the threshold reference values contained in each reagent kit as follows: urea reference value 11.32-40.3mg/dL, creatinine 0.7-1.1mg/dL for Women and 0.96-1.33mg/dL for man, ALT 7-35 UI/L for women and 10-40 IU/L for man, AST 13-35 IU/L for woman and 15-40 UI/L for man; ALP: 35-105 IU/L for woman and 40-130 UI/L for man, total bilirubin: 3.4-20.5 µmol/L woman and man, CKMB: <7 ng/mL woman and man, red blood cell: 3800000- 5000000/µL for women and 4,000000-6000000/µL for men; hemoglobin 10.5-15 g/L for women and 12.5-15 g/L for men, platelet <150000/µL woman and man and white blood cell <10000/µL woman and man. For the Neutrophil/Lymphocyte ratio, the pathological value defining COVID-19 infection was defined as a threshold greater than or equal to 2 [11].

Statistical analysis: Data collected on a data collection form were encoded using Epidata software version 3.1 and exported to SPSS version 25 for statistical analysis. Qualitative data were represented as absolute and relative frequencies (%), and quantitative data as means \pm standard deviation (SD) (if normal distribution) or median & interquartile range (IQR) (if skewed distribution). Pearson's Chi-square test or Fischer's Exact test were used to compare proportions. Student's t-test was used to compare the means of two groups with normal distributions. Man & Whitney's U test was used to compare the medians of two groups with asymmetric distributions, while Kruskal Wallis' H test was used to compare the medians of more than 2 groups.

The normal distribution of each variable was assessed using the Kolmogorov-Smirnov test. Outliers were identified using Tukey's robust approach [12] (Tukey limits). This method identifies extremes using the central 50% of the distribution, thus eliminating the confounding effects of a larger number of outliers, and involves calculating

(from the transformed data) the lower and upper quartiles (Q1 and Q3: i.e. 25th and 75th percentiles) from which the interquartile range (IQR) is calculated. Finally, the lower and upper limits (Tukey limits) were calculated as follows: the lower limit corresponds to $Q1 - 1.5 \times IQR$ and the upper limit to $Q3 + 1.5 \times IQR$. Any data point outside the Tukey limits was considered an extreme/outlier and removed from the analysis (i.e. discarded) [11]. As it has been established that the number of subjects can be reduced using parametric statistics (but that the data must have a Gaussian distribution), parametric analysis was first applied to the data. The central 90% (percentiles 2.5-97.5) of the distribution were taken into account to calculate the reference interval. From these data, a linear correlation between individual age, ALT and AST was found. To investigate the factors associated with the neutrophil/lymphocyte ratio, the stepwise logistic regression test was used, together with the calculation of ORa, to estimate the degree of association. The value of $p < 0.05$ will be used as the threshold of statistical significance.

RESULTS

The socio-demographic characteristics of the study population are illustrated in Table 1 and show that the mean age was 47.5 ± 16.0 years. Men were more represented (69.3%) with a sex ratio of 3H/1F. 28.9% of the study population were healthcare professionals and 26.9% had comorbidities (Table 1).

Table 1: Socio-demographic characteristics of the study population (N =1500)

Variable	Participants (%)
Mean age and standard deviation	47.5 \pm 16.0
Age range	
18-39 years	549 (36.6)
40-59 years	528 (35.2)
≥ 60 years	423 (28.2)
Gender	
Male	1041 (69.3)
Female	459 (30.6)
Profession	
Healthcare worker	434 (28.9)
Non-Healthcare worker	1066 (71.1)
Comorbidity	
No	1096 (73.1)
Yes	404 (26.9)

The results of the analysis of hematological and biochemical characteristics, after exclusion of outliers, are reported in Table 2. We measured seven biochemical parameters (creatinine, urea, Alanine-Amino-Transferase (ALT), Aspartate-Amino-Transferase (AST), Alkaline Phosphatase (ALP), total bilirubin and creatine kinase in myocardial blood (CK-MB)) and nine haematological parameters (red blood cell (RBC), haemoglobin (Hb), haematocrit (Hct), platelet, white blood cell, neutrophil, lymphocyte, monocyte and eosinophil).

Table 2: Biological characteristics of the study population

Variable	Mean	SD	RI Percentiles		90% LL of RI	90%UL of RI	Median	IQR (%)
			2.5	97.5	2.5%	97.5%		
Creatinine (mg/dL)	1.12	1.01	0.70	1.23	(0.61; 0.84)	(0.72; 1.81)	0.96	0.90-1.22
Urea (mg/dL)	71.4	25.5	13.6	118.5	(11.7; 15.4)	(116.6; 120.3)	72.4	58.9-85.4
ALT (UI/L)	26.5	25.7	7.9	81.2	(6.0; 9.8)	(79.3; 85.9)	19.6	13.9-30.2
AST (UI/L)	32.6	23.4	14.7	74.2	(13.0; 16.4)	(72.5; 75.9)	27.8	22.1-36.0
ALP (UI/L)	63.5	29.4	26.7	149.5	(24.5; 28.8)	(147.3; 151.6)	57.5	45.0-73.5
T. Bilirubine (μmol/L)	8.1	11.0	0.2	40.7	(-0.6; 1.0)	(39.9; 41.5)	1.4	0.5-13.4
CK-MB (ng/mL)	3.7	6.4	3.0	6.6	(2.5; 3.5)	(6.2; 7.1)	3.0	3.0-0.4
RBC x10 ⁶ /μL	5.0	1.2	3.5	6.1	(2.8; 4.3)	(5.4; 6.9)	4.7	4.3-5.1
Haemoglobin g/L	14.8	12.7	9.9	17.6	(9.0; 10.8)	(16.7; 18.6)	13.5	12.4-14.6
Haematocrit %	41.8	11.0	29.9	52.3	(29.1; 30.7)	(51.5; 53.1)	41.5	38.0-45.0
Platelet x10 ³ /μL	218.5	73.2	60.5	357.0	(55.2; 65.8)	(351.6; 362.3)	214.0	174.3-260.0
WBC x10 ³ /μL	9.3	40.6	3.3	10.0	(0.4; 6.3)	(7.1; 13.0)	5.6	4.8-6.7
Neutrophils x10 ³ /μL	3.6	9.6	1.2	6.9	(0.5; 1.9)	(6.2; 7.6)	2.5	1.9-32
Lymphocyte x10 ³ /μL	3.6	13.8	1.2	5.3	(0.2; 2.2)	(4.2; 6.3)	2.3	1.9-2.9
RNL	1.33	2.08	0.41	3.13	(0.26; 0.56)	(2.98; 3.28)	1.05	0.78-1.44
Monocytes x10 ³ /μL	0.9	5.2	0.2	1.3	(-0.2; 0.6)	(0.9; 1.7)	0.4	0.3-0.6
Eosinophils x10 ³ /μL	0.3	0.7	0.0	1.4	(0.0; 0.1)	(1.4; 1.5)	0.2	0.1-0.4

RI: reference interval; LL: lower limit; UL: upper limit; IQR: interquartile range; SD: standard deviation.

Table 3: General characteristics of the study population as a function of age

Variables	18-39 years (n=549)	40-59 years (n=528)	≥60 years (n=422)	P
Gender				
Male	373(67.9%)	368(69.8%)	299(70.7%)	0.626
Female	176(32.1%)	159(30.2%)	124(29.3%)	
Profession				
Healthcare worker	151(27.5%)	175(33.1%)	108(25.5%)	0.024
Non-Healthcare worker	398(72.5%)	353(66.9%)	315(74.5%)	
Comorbidity				<0.001
No	527(96.0%)	290(73.9%)	179(42.3%)	0.756
Yes	22(4.0%)	138(26.1)	244(57.7)	
Creatinine (mg/dL)	0.51(0.41-9.21)	0.96(0.90-1.22)	1.12(0.84-1.26)	0.684
Urea (mg/dL)	73.0(58.7-85.3)	72.9(59.4-85.8)	70.8(58.7-85.5)	0.035
ALT (UI/L)	20.3(14.4-32.5)	19.3(14.1-30.2)	18.5(13.3-28.2)	0.005
AST (UI/L)	28.4(22.9-37.2)	28.8(21.8-36.1)	26.1(21.2-34.5)	0.704
ALP (UI/L)	57.9(45.0-71.3)	57.9(45.1-75.9)	57.3(44.9-71.6)	0.042
T. Bilirubine (μmol/L)	2.2(0.6-13.7)	1.3(0.5-13.4)	1.1(0.5-13.0)	0.212
RBC x10 ⁶ /μL	4.7(4.3-5.1)	4.6(4.3-5.1)	4.7(4.3-5.2)	0.718
Haemoglobin g/L	13.6(12.4-14.7)	13.5(12.3-14.5)	13.4(12.4-14.6)	0.674
Haematocrit %	41.7(37.9-45.2)	41.5(37.7-44.8)	41.4(38.3-45.2)	0.529
Platelet count x10 ³ /μL	211.0(174.5-259.0)	214.0(171.0-258.8)	218.0(170.0-268.0)	0.156
WBC x10 ³ /μL	5.5(4.7-6.7)	5.8(4.9-6.7)	5.6(4.8-6.7)	0.255
Neutrophils (%)	43.8(37.4-50.9)	44.7(37.7-52.2)	43.8(36.0-51.6)	0.935
Lymphocyte (%)	42.3(36.4-48.2)	41.7(34.8-48.1)	42.1(34.6-49.6)	0.925
Monocytes (%)	7.5(5.9-9.9)	7.5(6.1-9.4)	7.3(5.7-9.0)	0.684
Eosinophils (%)	3.4(1.8-6.1)	3.1(1.7-5.7)	3.1(1.6-5.5)	

The results of the parametric analysis are presented as the mean, standard deviation (SD), reference interval (RI) (2.5-97.5%) and 90% confidence interval (CI) at the lower and upper limits of the RI. Non-parametric analysis of results includes median and interquartile range (25-75%) (Table 2).

The general characteristics of the population as a function of age were comparable ($p>0.05$), with the exception of the proportion of healthcare professionals, which was significantly higher in the 40-49 age group ($p=0.024$). The proportion of co-morbidities increased significantly with age ($p<0.001$). Median values for AST and ALT decreased significantly with increasing age ($p<0.05$), while total bilirubin levels decreased significantly

with increasing age (table 3).

Figures 1 and 2 illustrate the simple linear correlation between AST, ALT and age. A significant inverse relationship was observed between age and AST on the one hand ($p=0.015$) (Figure 1); and age and ALT on the other ($p=0.011$) (Figure 2). This correlation was 46.3% ($r=0.463$) for AST (Figure 1) and 46.9% for ALT (Fig 2).

Pathological values of biochemical and haematological parameters according to age were comparable, with the exception of the frequency of pathological ALT and AST, which was significantly higher in individuals aged 18-39 ($p<0.05$), while the frequency of pathological haemoglobin was significantly higher in individuals aged over 60 (Table 4).

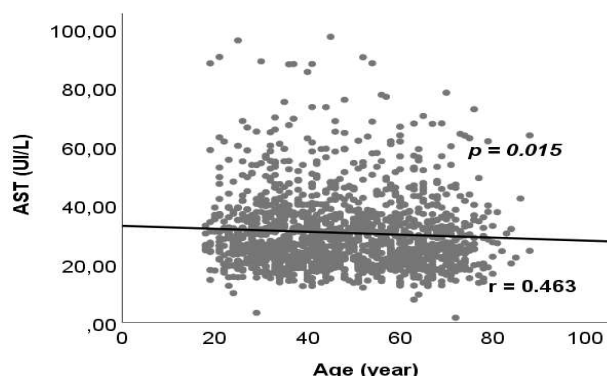


Figure 1: Linear correlation between AST and individual age

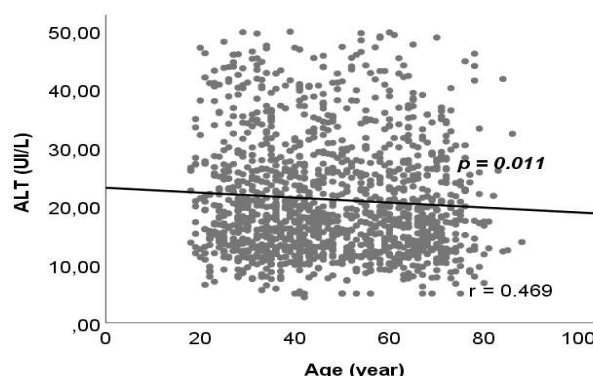


Figure 2: Linear correlation between ALT and individual age

Table 4: Assessment of abnormal values of biochemical and haematological parameters as a function of age

Variable	Over all (n=1500)	18-39 years (n=549)	40-59 years (n=528)	≥60 years (n=423)	P value
Abnormal creatinine	23(1.5)	13(2.4)	6(1.1)	4(0.9)	0.163
Abnormal urea	143(9.5)	51(9.3)	54(10.2)	38(9.0)	0.778
ALT pathological	165(11.0)	67(12.2)	58(11.0)	40(9.5)	0.043
AST pathological	194(12.9)	75(13.7)	72(13.6)	47(11.1)	0.041
ALP pathological	108(7.2)	37(6.7)	37(7.0)	34(8.0)	0.724
Total Bilirubin pathological	146(9.7)	55(10.0)	59(11.2)	32(7.6)	0.167
CK-MB pathological	34(2.3)	10(1.8)	14(2.7)	10(2.4)	0.641
RBC pathological	180(12.0)	70(12.8)	68(12.9)	42(9.9)	0.295
Hb Pathological	319(21.3)	111(20.2)	114(21.6)	94(22.2)	0.023
Hct pathological	288(19.2)	102(18.6)	111(21.0)	75(17.7)	0.391
Platelet pathological	190(12.7)	66(12.0)	69(13.1)	55(13.0)	0.856
WBC Pathological	37(2.5)	11(2.0)	14(2.7)	12(2.8)	0.679
Neutrophil pathological	23(1.5)	8(1.5)	7(1.3)	8(1.9)	0.778
Lymphocyte pathological	37(2.5)	13(2.4)	11(2.1)	13(3.1)	0.619
RNL≥2	143(9.5)	44(8.0)	54(10.2)	45(10.6)	0.300
Monocyte pathological	609(40.6)	232(42.3)	221(41.9)	156(36.9)	0.182
Eosinophil pathological	105(7.0)	41(7.5)	37(7.0)	27(6.4)	0.809

RNL: Ratio Neutrophile-Lymphocyte

A total of 143 individuals, or 9.5% of those presenting for vaccination, had an $RNL \geq 2$, indicating a COVID-19 infection. Comparing individuals with $RNL < 2$ to those with $RNL \geq 2$, it was noted that women ($p=0.022$), individuals with comorbidity ($p=0.026$), those with pathological WBC count ($p=0.005$), those with pathological RBC count ($p=0.004$), and those with pathological platelet count had a significantly higher frequency of $RNL \geq 2$ (Table 5).

Analysis of this table had shown that female gender, the presence of comorbidity and the presence of abnormal ALP, the presence of abnormal RBC and the presence of abnormal platelet had emerged as factors associated with the stigma of COVID-19 infection ($RNL \geq 2$). After multivariate adjustment of these variables, only female gender (aOR : 2.94 IC95%: 1.99-3.96), presence of comorbidity (aOR: 2.83 IC95%: 1.88-3.88), presence of abnormal PAL (aOR: 2.12 IC95%: 1.24-3.62) and the presence of abnormal RBC (aOR: 1.92 IC95%: 1.22-3.01) had persisted as factors independently associated with the stigma of COVID-19 infection in the study population (Table 6).

Table 5: General characteristics of the study population according to RNL

Variable	RNL<2 (n=1357)	RNL≥2 (n=143)	P
Age			0.300
18-39 years	505(37.2)	44(30.8)	
40-59 years	474(34.9)	54(37.8)	
≥60 years	378(27.9)	45(31.5)	
Gender			0.022
Male	952(70.2)	88(61.5)	
Female	404(29.8)	55(38.5)	
Profession			0.486
Healthcare worker	392(28.9)	42(29.4)	
Non-Healthcare worker	965(71.1)	101(70.6)	
Comorbidity			0.026
Abnormal creatinine	21(1.5)	2(1.4)	0.622
Abnormal urea	130(9.6)	13(9.1)	0.497
ALT pathological	149(11.0)	16(11.2)	0.514
AST pathological	174(12.8)	20(14.0)	0.387
ALP pathological	89(6.6)	19(13.3)	0.005
Bilirubin T pathological	134(9.9)	12(8.4)	0.347
CKMB pathological	32(2.4)	2(1.4)	0.356
GR pathological	152(11.2)	28(19.6)	0.004
Hb pathological	283(20.9)	36(25.2)	0.138
Hct pathological	256(18.9)	32(22.4)	0.182
Platelet pathological	165(12.2)	25(17.5)	0.020

Table 6: Factors associated with the stigma of COVID-19 infection (RNL \geq 2)

Variable	Univariate analysis		Multivariate analysis	
	p	cOR (95%CI)	p	aOR (95%CI)
Sex				
Male		1		1
Female	0.033	2.47(1.03-3.10)	0.016	2.94 (1.99-3.96)
Comorbidity				
No		1		1
Yes	0.014	2.32(1.91-2.92)	0.019	2.83(1.88-3.88)
ALP				
Normal		1		1
Abnormal	0.004	2.18(1.29-3.70)	0.006	2.12(1.24-3.62)
RBC				
Normal		1		1
Abnormal	0.004	1.93(1.24-3.02)	0.005	1.92(1.22-3.01)
Platelet				
Normal		1		1
Abnormal	0.037	1.53(1.19-2.43)	NS	-

DISCUSSION

The aim of this study was a pre-vaccination profile assessment to identify risks for adverse events. The results showed that the majority of the population was composed of young adults aged between 18 and 59. The mean age of the population was 47.5 \pm 16.0 years, with extremes ranging from 18 to 88 years, and the majority were male (69.3%). The age found in this study corroborates with the study by Bulaba M et al on the epidemiological profile of people fully vaccinated against COVID-19 in Kinshasa: case the Gombe Vaccine Center, May 2022, who had found a higher frequency of individuals under 50 years of age (78.6%) and fewer individuals of the female sex (37.0%). [13] Another study carried out by Mpoyi T and Kabamba M in Lubumbashi had shown the same trend with an over-representation of men and individuals whose average age was 33.3 [14]. It could be said that the results of our study, with a predominance of young people under the age of 50 (78.6%) and a low representation of women (37.0%), are consistent with the profiles observed elsewhere in the DRC [13,14], showing that more than 52% of those vaccinated were aged 18 to 25, and that they were predominantly men (50.4%). Furthermore, the study conducted by Mpoyi T and Kabamba M in Lubumbashi revealed that vaccine hesitancy was more prevalent among women and people under 35 [14], further highlighting the underrepresentation of women observed in our population. This finding is due to the fact that young men are often over-represented in sectors such as health, security, transport or trade, which are the key sectors where vaccination was a priority. The DRC's professional environment or higher education establishment had required vaccination, and young adults, often still in these environments, had to comply. [15]

The health work in this study represented only 28.9%. This frequency is high compared with that of Lubalu M et al, who had reported a frequency of 4.6% of vaccinated healthcare professionals in Kinshasa in 2022. [13]

This difference can be explained by several contextual factors. First, our study was conducted in a vaccination center located in university clinics, which brings together many healthcare professionals, unlike the study by Lubalu M et al., which appears to have been conducted in an area with lower healthcare density. In addition, our survey period corresponded to a phase of vaccination targeting healthcare professionals. The low level of vaccination of healthcare professionals against COVID-19 observed in certain contexts may seem paradoxical, but it can be explained by a complex set of individuals, institutional and social factors. Mistrust of the rapid development of vaccines against COVID-19, uncertainty about long-term side effects, especially with new technologies such as mRNA, doubt about the efficacy of vaccines against emerging variants and the influence of fake news or contradictory scientific information may also explain the low vaccination of healthcare professionals against COVID-19. [16,17]

The application of an appropriate Reference Interval (RI) is a major challenge for the DRC, particularly for common or most requested biochemical and haematological parameters, as published RIs are generally derived from the developed Western world where populations and disease profiles differ. In our study, the reference ranges for creatinine, urea, Alanine-Amino-Transferase, Aspartate-Amino-Transferase, Alkaline Phosphatase, Total Bilirubin, Creatine kinase in myocardial blood and nine haematological parameters (red blood cell, haemoglobin, haematocrit, platelet, white blood cell, neutrophil, lymphocyte, monocyte and eosinophil) showed values close to those found in the African literature. Mendieta-Gutiérrez C et al, reported 95% reference ranges for leukocytes from 4.9.10³ to 10.9.10³/mm³ for man and 4.9.10³ to 10.7.10³/mm³ for woman; for red blood cells from 5.03.10⁶ to 6.36.10⁶/mm³ for man and 4.35.10⁶ to 5.75.10⁶/mm³ for woman; and for platelets from 175.10³ to 388.10³/mm³ for man and 185.10³ to 386.10³/mm³. [18] It is important to report these reference intervals, to provide practitioners in the DRC with their own values so that they can no longer resort to values from other countries or Westerners.

In this study, we found a simple linear correlation between age of vaccinees, AST and ALT. These two correlations explained a respective relationship of 46.3% and 46.9%. This correlation in both variables was significant and negative, explaining a decrease in AST and ALT values with increasing age. This could be explained by the fact that, with age, the total mass of the liver progressively decreases. It turns out that the reduction in active liver tissue naturally leads to a reduction in the production and release of these enzymes into the bloodstream. As the liver becomes less metabolically active with aging, this is accompanied by a decrease in the expression of liver enzymes, including AST and ALT. [19-21]

The frequency of individuals with suspected COVID-19 infection (RNL \geq 2) was 9.5%. This frequency is close to that reported in the African literature, where capacities for this infection were highly variable from country to

country but did not exceed in the community 3.2% in North Africa and 2.7% in South.[22,23] Factors associated with the stigma of COVID-19 infection were female gender (aOR: 2.94 IC95%: 1.99-3.96), presence of comorbidity (aOR: 2.83 IC95%: 1.88-3.88), presence of abnormal PAL (aOR: 2.12 IC95%: 1.24-3.62) and presence of abnormal RBC (aOR: 1.92 IC95%: 1.22-3.01). Several studies have reported that women may account for a greater proportion of COVID-9-positive cases in certain cohorts. [24-26] And this may be because female hormones (such as estrogen) can have a protective effect by boosting the immune response. Women often have a more robust immune response, thanks in part to genetics (for example, genes involved in immunity are located on the X chromosome), this means that clinical signs may not manifest and be discovered incidentally during vaccination check-ups.[26] The presence of comorbidities influences the occurrence of COVID-19 because they weaken the body and diminish its ability to fight infection effectively. So, comorbidities make the body more vulnerable to the severe effects of COVID-19, increasing the risk of serious complications and death.[27] The mechanism by which LAP influences COVID-19 stigmatization is controversial, but it may be a sign of at-risk terrain, i.e. a physiological condition (such as liver disease) that makes disease progression potentially more severe. Abnormal red blood cell count may influence the severity of COVID-19, especially in relation to oxygenation and thromboembolic risks.

LIMITATIONS

As this is a cross-sectional study, it is not possible to determine whether exposure ($RNL \geq 2$) precedes the effect. Therefore, it is impossible to determine a clear causal relationship among the factors associated with stigma to COVID-19 infection. People who attended the vaccination site may have differed from those who did not (age, socio-economic level, access to healthcare...), so it is impossible to generalize the results of the study. Another limitation is selection bias, given that the participants involved in the study were volunteers from one site, they may not be representative of the population of the DRC. The lack of information on certain variables, such as history of COVID-19 infection, may lead to potential confounding bias. Finally, the data collected may be inaccurate, especially if they depend on the subjective statements of participants or on less-than-rigorous data collection.

CONCLUSION

During the COVID-19 era, several individuals came to the Clinique Universitaire de Kinshasa vaccination center. Their profile was assessed and matched the majority of profiles found in the literature, and the majority had no biological abnormalities that could hinder vaccination. These results were essential, as they enabled a decision to be taken to vaccinate a large number of individuals at

the vaccination site and achieve high coverage among this high-risk group. Under these circumstances, we suggest incorporating systematic NLR screening in individuals belonging to high-risk groups (the elderly, those with comorbidities, exposed professionals) prior to vaccine administration. This would enable the identification of any pre-existing inflammation or immune imbalances that could influence the response to the vaccine or indicate an ongoing subclinical infection.

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Availability of Data: The datasets during the current study are available from the corresponding author upon reasonable request via mail on nkodilaaliocha@gmail.com in case of need for a possible verification.

Declaration of Non-use of generative AI Tools: This article was prepared without the use of generative AI tools for content creation, analysis, or data generation. All findings and interpretations are based solely on the authors' independent work and expertise.

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