ABO/Rh Blood Groups and COVID-19: Temporal Analyses Point Out

Rh-negative with the Greatest Correlations

Preliminary statistical studies external to the hospitals

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Abstract

In this work, the correlations between ABO/Rh blood groups and the number of deaths from COVID-19 were studied through Pearson's correlation coefficients, while considering the distribution of blood groups in populations of 88 countries for a period of 166 days and the daily cumulative deaths since the fifth death. The current study stems from the need to understand associations between ABO/Rh blood groups and COVID-19 in a temporal analysis. The preliminary results indicated that correlations change statistically as the pandemic extends and the time of exposure to the SARS-CoV-2 increases. A strong maximum correlation was obtained for blood groups A, O, A-, O-, Rh- and blood group A correlations were higher than those of the O blood group during most of the study period. Correlations of the blood type Rh-negative remained greater than those of the blood type Rh-positive throughout the 166-day period. With these studies it was possible to interpret the temporal evolution of the pandemic from the perspective of the correlation coefficients, here modeled by degree 11 polynomials using the least squares method. In addition, the behavior of the temporal evolutions of the correlations suggested studies on the total number of daily deaths, so rates of establishment of the pandemic COVID-19 and characterization parameters were proposed.

Keywords: COVID-19, SARS-CoV-2, ABO, Rh, blood group, correlation.

INTRODUCTION

This research is based on the principle that with advent of COVID-19 pandemic, humanity was subject to SARS-CoV-2 in a natural way, with virus acting freely during the study period, without an accessible, direct and effective combat through vaccines or medication. The reactions to the viral load are related at first glance to the response of the immune system of each individual, health care in hospital settings and of the speed of proliferation of the virus associated with the contagious conditions. In this way, we can define the existence of two active factors: a biological and a social one. Studies associating COVID-19 with blood groups have been conducted in hospital settings with a control population in Wuhan and Shenzhen, by Zhao [1], in New York by Zietz [2] (April 5, 2020) and Latz [3] from March 6 to April 16, 2020. Ellinghaus [4] in genetic studies obtained results that supported previous work. However, because it is something new to the scientific field, many research gaps need to be addressed in addition to hospital settings, in this sense, works for a single date were carried out by Alkout [5] (April 13, 2020) and Takagi [6] (June 25, 2020). In our work, presented here, the studies were extended to a period of 166 days.

The immune system in some cases is associated with the blood group of individuals as described by Mourant [7] and Mattos [8]. In this context, clinical studies of the severe acute respiratory syndrome coronavirus (SARS-CoV-1) Cheng [9] concludes that the blood type interferes with the level of susceptibility to viral attack, Chen [10] suggests the existence of a great similarity between SARS-CoV-1 and the SARS-CoV-2. In Wuhan and Shenzhen, Zhao [1] observed that A blood group presents a higher risk of contamination and death by COVID-19 when compared to the local population and O blood group with some protection. Zietz [2] and Latz [3] also concluded that A blood group would be more likely to contract the virus than O blood group, but without evidence of associations for serious cases or deaths. In clinical studies for the period from March 16 to May 20, 2020, Arac [11] suggested that the Rh-positive (Rh+) blood group has a significant predisposition and Rh-negative (Rh-) has protection to COVID-19.

This paper intends to contribute to the broad view of the temporal process of the COVID-19 pandemic, so it focuses on environments external to the hospitals. The Pearson's correlation coefficients were calculated day-to-day between the number of cumulative deaths since the fifth death and the number of individuals of each blood type of the considered countries, spread over a period of 166 days. Analyzing the cumulative data since the fifth death, it is expected that the countries chosen in some way have equal temporal exposure to SARS-CoV-2.

The data was treated with logarithmic transformations. Pearson's correlations was used to analyze four countries sets. From 88 countries (Analysis 1) and another from 88 countries without China and India (Analysis 2), similar maximum correlations (ρ) were obtained for blood groups A ($\rho = 0.75$, p-value = 0.00, CI = [0.64 0.99]), O ($\rho = 0.76$, p-value = 0.00, CI = [0.43 0.98]), A-negative (A-) ($\rho = 0.73$, p-value = 0.00, CI = [0.73 0.99]) and O- negative (O-) ($\rho = 0.77$, p-value = 0.00, CI = [0.70 0.99]), with blood group A being greater than blood group O for most of the analyzed period, finally for Rh- ($\rho = 0.73$, p-value = 0.00, CI = [0.71 0.99]). For the set without China, India and the most affected countries (Analysis 3), the maximum moderate correlations were A ($\rho = 0.65$, p-value = 0.00, CI = [0.64 0.99]) and O ($\rho = 0.69$, p-value = 0.00, CI = [0.43 0.98]). For these three sets of countries the correlations of the ABO/Rh-negative were higher than those of the ABO/Rh-positive blood groups. For blood types AB-positive (AB+) and B-positive (B+) weak correlations were found and blood type Rh-correlations remained greater than those of the blood type Rh+ throughout the 166-day period. In the analysis of the set of countries most exposed (Analysis 4), all ABO and Rh blood groups, regardless of the Rh factor, showed very strong maximum correlations and a parallelism of the correlations and p-

values between blood type Rh+ and Rh- with a 14 days lag, which owes a possible relationship between Rh blood types from an epidemiological perspective.

The temporal evolutions of the correlation coefficients were modeled with degree 11 polynomials. Characterization parameter was defined in relation to the speed of pandemic expansion. Additionally, based on the number of daily deaths in the countries, parameters of characterization of the COVID-19 were established with degree 7 polynomials.

The results presented have greater relevance as complementary studies from other areas of knowledge (genetics, clinical and epidemiological) to support them. These results do not necessarily reveal a causal relationship, but that there are correlations that may not be directly related to the cause of deaths and active in a broader scope of the pandemic from an epidemiological point of view.

METHODS

Blood donation collection sites monitor the distribution of blood types in each country. Thus, the number of individuals of each blood type from 88 different countries was calculated from the data obtained at http://www.rhesusnegative.net/themission/bloodtypefrequencies. The data referring to the from SARS-CoV-2 cumulative number of deaths up to 8/19/2020 is available at https://ourworldindata.org/covid-deaths, which is maintained by the European Center for Disease Prevention and Control (ECDC). With these data, the daily correlations were calculated between the number of cumulative deaths and the number of individuals in the ABO and Rh blood groups, for the period of 166 days from the fifth death of each of the considered countries. The statistical tool used was Pearson's correlation coefficient with logarithmic transformation data justified in Feng [12]. The analysis was performed with the aid of the Kmeans MacQueen algorithm [13] to suggest the sets of countries.

Table 1 shows the four sets of countries, where the daily correlations between the number of deaths and the number of individuals in the ABO/Rh+, ABO/Rh-, ABO and Rh blood groups were calculated.

Total correlations = 166 days x 4 analyses x 14 blood groups = 9246

Total deaths in 166 days = 754334, distributed among 88 countries

Table 1: Analyses considering data treatment with logarithmic transformations, for subsets of countries referring to Table 9 in the Appendix.

Analyses	Countries	Deaths (%)
1	88 countries	100
2	88 countries except China and India	92.4
3	88 countries except Belgium, Brazil, China, France, India, Italy, Mexico, Spain, United Kingdom and USA	28.5
4	Belgium, Brazil, France, Italy, Mexico, Spain, United Kingdom and USA	63.9

The computational tool used was the R software on a Linux operating system from the Fedora distribution. The data were compared using p-value test (Kim [14]), and normality tests (Feng [12]) were also performed. The least squares method was used to model the temporal evolutions of the correlations with degree 11 polynomials and parameters of characterization of the pandemic were established with degree 7 polynomials.

RESULTS

Considering pandemic's data provided by Our World in Data, Graph 1 shows numbers of countries at *x* days since the fifth death, while considering the deadline of 19/08/2020. When the periods of days since the fifth death are used, it is intended to align all countries to the same degree of exposure to the pandemic. For example, in Graph 1, 150 days since five deaths 37 countries are exposed.

During the first few days, there is statistical instability due to the quality of the samples. When the number of days approaches to 150, it begins another period of instability where the samples have few exposed countries.

Correlations with the following references were considered in absolute values (abs):

weak: $0 < abs(\rho) \le 0.5$, moderate: $0.5 < abs(\rho) \le 0.7$, strong: $0.7 < abs(\rho) \le 0.9$, very strong: $0.9 < abs(\rho) \le 1$





Graph 1 – Pandemic in 2020-08-19 through the number of countries (y-axis) that have x days since the fifth reported death (x-axis).

The Analyses 1-4 shown in Table 1 were performed with logarithmic transformations of the following data: population of each country, respective absolute proportions of blood types, number of deaths in each country. Logarithmic transformations decrease variability, population differences and

normalize the data set (Feng [12]), so with this data treatment it is possible to employ Pearson's correlations.

The results of the maximum correlations, were obtained at the end of period analyzed, with the respective p-values shown in Table 2; the considered temporal intervals of the Analyses 1-4 are respectively: [35, 120], [35,120], [35,120], [35,140].

Table 2 – Statistics from Analyses 1-4: maximum correlation coefficients (ρ) for the temporal intervals [35, 120], [35,120], [35,140], respective p-values and Confidence Intervals (CIs).

		A	÷		0-	+		B	÷		AB	+		Rh+ Facto	r
	ρ	p-value	95% C.I.	ρ	95% C.I.	p-value									
1	0.67	0.00	[-0.63 0.77]	0.66	0.00	[-0.65 0.75]	0.50	0.00	[0.10 0.95]	0.53	0.00	[0.34 0.97]	0.60	[0.37 0.97]	0.00
2	0.66	0.00	[-0.63 0.77]	0.65	0.00	[-0.65 0.75]	0.48	0.00	[0.10 0.95]	0.52	0.00	[0.34 0.97]	0.59	[0.37 0.97]	0.00
3	0.59	0.00	[-0.63 0.77]	0.59	0.00	[-0.65 0.75]	0.43	0.00	[0.10 0.95]	0.47	0.00	[0.34 0.97]	0.53	[0.37 0.97]	0.00
4	0.99	0.00	[-0.60 0.78]	0.97	0.00	[-0.87 0.40]	0.99	0.00	[-0.20 0.91]	0.98	0.00	[0.26 0.97]	0.99	[0.77 0.99]	0.00
		A			0	-		B	-		AB	-		Rh- Facto	r
	ρ	p-value	95% C.I.	ρ	95% C.I.	p-value									
1	0.73	0.00	[0.73 0.99]	0.77	0.00	[0.70 0.99]	0.66	0.00	[0.76 0.99]	0.66	0.00	[0.92 1.00]	0.73	[0.71 0.99]	0.00
2	0.72	0.00	[0.73 0.99]	0.76	0.00	[0.70 0.99]	0.65	0.00	[0.76 0.99]	0.65	0.00	[0.92 1.00]	0.72	[0.70 0.99]	0.00
3	0.61	0.00	[0.91 1.00]	0.68	0.00	[0.70 0.99]	0.56	0.00	[0.76 0.99]	0.55	0.00	[0.92 1.00]	0.63	[0.71 0.99]	0.00
4	0.94	0.00	[0.70 0.99]	0.97	0.00	[0.69 0.99]	0.95	0.00	[0.10 0.95]	0.91	0.00	[0.91 1.00]	0.95	[0.16 0.96]	0.00
		Α			0			В			AB	5			
	ρ	p-value	95% C.I.												
1	0.75	0.00	[0.64 0.99]	0.76	0.00	[0.43 0.98]	0.61	0.00	[0.60 0.98]	0.64	0.00	[0.72 0.99]			
2	0.74	0.00	[0.64 0.99]	0.76	0.00	[0.43 0.98]	0.60	0.00	[0.60 0.98]	0.63	0.00	[0.72 0.99]			
3	0.65	0.00	[0.64 0.99]	0.69	0.00	[0.43 0.98]	0.53	0.00	[0.60 0.98]	0.56	0.00	[0.72 0.99]			
4	0.98	0.00	[0.49 0.98]	0.99	0.00	[0.77 0.99]	0.99	0.00	[0.60 0.98]	0.95	0.00	[-0.02 0.94]			

Table 2 shows that in Analysis 1 similar maximum correlations were obtained for blood group A ($\rho = 0.75$, p-value = 0.00, CI = [0.64 0.99]), O ($\rho = 0.76$, p-value = 0.00, CI = [0.43 0.98]), A- ($\rho = 0.73$, p-value = 0.00, CI = [0.73 0.99]) and O- ($\rho = 0.77$, p-value = 0.00, CI = [0.70 0.99]), finally for Rh- ($\rho = 0.73$, p-value = 0.00, CI = [0.71 0.99]). In Analysis 3, the maximum moderate correlations were A ($\rho = 0.65$, p-value = 0.00, CI = [0.64 0.99]) and O ($\rho = 0.69$, p-value = 0.00, CI = [0.43 0.98]). Between Analyses 1, 2 and 3 there are little variations in the correlation coefficients, due to the logarithmic transformations of the data. In Analysis 4 very strong coefficients are presented.

The coefficients of the ABO- and Rh- Factor blood groups have small Confidence Intervals (CI), that denote a greater precision of the correlation coefficients, except in Analysis 4 of the Rh- (CI = $[0.16 \ 0.96]$) and B- (CI = $[0.10 \ 0.95]$). ABO+ blood types presented higher Confidence Intervals, blood types A+ and O+ (Analysis 1-4) and B+ (Analysis 4) contain value of 0 which makes the results inaccurate and statistically unreliable.

Tables 3-6 refer to polynomial modeling through least squares method of the correlations temporal evolutions of Analyses 1-4, respectively, the degree 11 polynomial (*P*) is given by:

 $P(t) = Intercept + I_1(t^1) + I_2(t^2) + \dots + I_{10}(t^{10}) + I_{11}(t^{11}),$

where t refers to the days since five deaths: $t = \{1, 2, 3, ...\}$.

In Tables 3-6 the standard deviation of the residue is given by StdErr and determination coefficient by R². The R² is a measure that allows to say how much the polynomial found represents the calculated correlation coefficients, the closer to the unit the better is the approximation.

Table 3 – Polynomial coefficients (n = 11) of the temporal evolution of the correlations were obtained by the least squares method, standard deviation of the residue (StdErr) and coefficient of determination (R^2) for Analysis 1 with logarithmic data.

					Analysis	1 – Loga	rithmic T	ransform	ations					
	Intercept	I_1	I_2	I_3	I_4	I_5	I_6	I ₇	I_8	I ₉	I ₁₀	I ₁₁	StdErr	\mathbb{R}^2
O +	-0.06	7.66	-84.38	593.23	-2513.66	6702.29	-11654.58	13420.17	-10150.00	4846.32	-1323.99	157.65	0.01	0.99
A+	0.01	7.69	-87.40	639.90	-2814.86	7754.81	-13881.35	16405.87	-12704.33	6198.13	-1727.36	209.54	0.01	0.99
B +	-0.04	5.28	-68.77	560.03	-2615.50	7490.10	-13806.98	16728.88	-13248.11	6599.31	-1875.46	231.74	0.01	0.99
AB^+	0.00	5.82	-70.50	549.06	-2509.31	7090.89	-12945.40	15567.72	-12255.53	6076.27	-1720.47	211.99	0.01	0.99
0-	-0.03	12.16	-142.33	995.40	-4181.11	11088.48	-19230.69	22116.01	-16713.36	7973.82	-2176.55	258.96	0.01	0.99
<i>A</i> -	0.03	11.85	-142.24	1033.28	-4515.69	12434.24	-22331.83	26528.77	-20661.80	10139.59	-2842.30	346.82	0.01	0.99
В-	-0.03	11.06	-139.61	1047.78	-4655.01	12928.29	-23332.71	27805.21	-21707.08	10673.97	-2997.66	366.43	0.01	1.00
AB-	-0.02	11.81	-148.50	1103.61	-4860.21	13359.73	-23818.83	28001.91	-21549.68	10442.80	-2890.21	348.24	0.01	0.99
0	-0.05	10.53	-119.59	832.20	-3484.95	9204.65	-15882.48	18161.92	-13644.27	6471.09	-1756.05	207.73	0.01	0.99
A	0.02	10.47	-122.18	883.46	-3847.63	10545.46	-18835.38	22244.61	-17224.00	8404.62	-2343.13	284.42	0.01	0.99
В	-0.04	8.50	-108.42	837.89	-3790.85	10643.24	-19344.76	23171.75	-18165.08	8964.23	-2525.43	309.56	0.01	1.00
AB	-0.01	9.39	-115.81	869.07	-3860.63	10684.02	-19166.52	22676.33	-17569.84	8575.42	-2391.07	290.27	0.01	1.00
Rh+	-0.02	6.71	-79.01	595.99	-2662.08	7397.65	-13322.65	15828.43	-12320.12	6042.03	-1692.76	206.43	0.01	0.99
Rh-	-0.01	12.07	-146.78	1068.05	-4642.33	12672.86	-22534.97	26496.70	-20429.80	9929.14	-2757.79	333.58	0.01	0.99

Table 4 – Polynomial coefficients (n = 11) of the temporal evolution of the correlations were obtained by the least squares method, standard deviation of the residue (StdErr) and coefficient of determination (R^2) for Analysis 2 with logarithmic data.

					Analysis	2 – Loga	rithmic T	ransform	ations					
	Intercept	I_1	I ₂	I ₃	I_4	I_5	I_6	I ₇	I_8	I_9	I 10	I ₁₁	StdErr	\mathbb{R}^2
O +	-0.14	7.77	-80.36	553.60	-2324.56	6159.60	-10655.53	12215.17	-9203.99	4381.22	-1194.06	141.92	0.02	0.99
A+	-0.06	7.88	-85.12	615.46	-2698.70	7424.81	-13279.02	15684.45	-12141.59	5923.27	-1651.12	200.39	0.01	0.99
B +	-0.14	5.60	-69.66	563.74	-2628.93	7520.25	-13850.59	16773.98	-13283.97	6620.24	-1882.99	232.94	0.01	0.99
AB+	-0.09	6.13	-70.76	545.14	-2481.74	6993.14	-12736.94	15289.75	-12022.96	5957.84	-1686.96	207.95	0.01	0.99
0-	-0.09	13.36	-156.24	1084.65	-4522.17	11913.79	-20542.77	23505.50	-17684.35	8403.89	-2285.94	271.13	0.01	0.99
A-	-0.01	12.69	-152.02	1097.26	-4768.04	13069.94	-23390.42	27708.67	-21532.96	10548.51	-2952.79	359.90	0.01	0.99
B -	-0.11	13.03	-164.77	1222.78	-5373.08	14785.84	-26482.63	31358.83	-24350.58	11919.69	-3334.64	406.29	0.01	0.99
AB-	-0.09	13.52	-170.31	1253.74	-5469.29	14913.63	-26409.94	30868.69	-23636.40	11403.27	-3143.62	377.44	0.01	0.99
0	-0.12	11.32	-125.75	863.24	-3578.89	9373.47	-16053.14	18232.96	-13613.24	6420.15	-1733.35	204.10	0.01	0.99
A	-0.04	11.14	-127.69	915.19	-3965.72	10832.22	-19299.87	22751.55	-17593.08	8576.79	-2389.75	289.99	0.01	0.99
В	-0.14	9.81	-123.59	943.86	-4232.34	11800.34	-21328.08	25430.84	-19861.45	9771.41	-2746.02	335.93	0.01	0.99
AB	-0.09	10.64	-129.59	961.17	-4230.02	11616.11	-20701.42	24351.90	-18773.30	9122.47	-2533.81	306.57	0.01	1.00
Rh+	-0.11	6.98	-78.12	582.45	-2592.25	7186.70	-12917.56	15323.38	-11913.98	5839.16	-1635.57	199.48	0.01	0.99
Rh-	-0.08	13.55	-165.02	1190.70	-5132.21	13909.96	-24585.74	28760.30	-22078.28	10690.05	-2959.51	356.98	0.01	0.99

Table 5 – Polynomial coefficients (n = 11) of the temporal evolution of the correlations were obtained by the least squares method, standard deviation of the residue (StdErr) and coefficient of determination (R^2) for Analysis 3 with logarithmic data.

					Analysis	3 – Loga	rithmic Ti	ransform	ations					
	Intercept	I_1	I_2	I_3	I_4	I_5	I_6	I_7	I_8	I_9	I_{10}	I 11	StdErr	\mathbb{R}^2
O +	-0.16	4.50	-33.95	225.75	-978.03	2696.29	-4853.97	5792.93	-4547.12	2255.18	-639.89	79.04	0.02	0.99
A+	-0.09	4.41	-36.97	287.75	-1407.62	4242.01	-8172.44	10278.35	-8402.06	4300.46	-1250.91	157.68	0.01	0.99
B +	-0.17	4.14	-50.44	442.19	-2194.46	6587.95	-12637.62	15866.65	-12981.35	6663.77	-1947.08	246.83	0.02	0.99
AB+	-0.12	4.50	-47.04	386.40	-1880.93	5594.94	-10663.77	13322.84	-10861.12	5562.10	-1622.95	205.62	0.01	0.99
0-	-0.11	8.98	-97.46	693.06	-2995.62	8158.22	-14487.68	17022.66	-13119.67	6373.24	-1768.53	213.57	0.01	0.99
<i>A</i> -	-0.03	8.33	-94.38	726.80	-3394.66	9890.56	-18616.10	23003.26	-18526.95	9357.84	-2689.42	335.35	0.01	0.99
В-	-0.15	9.98	-126.59	994.58	-4595.96	13171.45	-24401.79	29746.56	-23695.41	11864.84	-3387.22	420.26	0.01	0.99
AB-	-0.13	11.03	-137.53	1051.28	-4755.10	13343.58	-24177.37	28801.56	-22415.94	10969.88	-3062.57	371.85	0.01	0.99
0	-0.15	7.19	-68.38	469.74	-2002.49	5395.31	-9482.58	11033.07	-8428.21	4062.40	-1119.64	134.40	0.02	0.99
A	-0.06	6.96	-70.80	541.11	-2544.66	7453.72	-14072.99	17420.84	-14047.69	7102.15	-2042.85	254.92	0.01	0.99
В	-0.17	7.35	-92.13	751.26	-3559.15	10365.23	-19428.13	23910.88	-19209.17	9694.11	-2787.79	348.24	0.01	0.99
AB	-0.14	8.33	-97.74	756.64	-3480.05	9905.76	-18184.56	21945.51	-17308.49	8586.68	-2430.63	299.24	0.01	0.99
Rh+	-0.14	4.50	-43.59	348.72	-1680.04	4971.43	-9441.69	11758.01	-9552.81	4873.64	-1416.11	178.59	0.02	0.99
Rh-	-0.11	9.96	-117.85	892.33	-4042.38	11421.00	-20899.41	25185.31	-19841.88	9829.85	-2777.33	341.13	0.01	0.99

Table 6 – Polynomial coefficients (n = 11) of the temporal evolution of the correlations were obtained by the least squares method, standard deviation of the residue (StdErr) and determination coefficient (R^2) for Analysis 4 with logarithmic data.

					Analysis	s 4 – Loga	rithmic T	ransforma	ations					
	Intercept	I_1	I_2	I_3	I_4	I ₅	I_6	I ₇	I_8	I_9	I 10	I 11	StdErr	\mathbb{R}^2
O +	0.65	-34.55	335.81	-1818.97	6393.03	-15011.51	23855.60	-25665.92	18380.47	-8379.50	2198.18	-252.41	0.03	1.00
A+	0.77	-35.30	328.31	-1667.74	5542.51	-12499.68	19339.77	-20462.84	14511.83	-6581.69	1722.77	-197.76	0.03	1.00
B +	0.72	-34.17	312.69	-1574.29	5218.80	-11777.82	18255.66	-19351.21	13743.14	-6238.78	1633.72	-187.54	0.03	1.00
AB+	0.84	-35.56	307.02	-1416.82	4336.98	-9241.00	13818.56	-14362.87	10110.92	-4580.08	1201.41	-138.43	0.03	1.00
0-	0.70	-25.06	181.39	-585.25	893.11	-42.71	-2314.67	4349.89	-4088.37	2193.74	-641.40	79.58	0.02	1.00
<i>A</i> -	0.79	-25.33	180.70	-542.04	645.36	617.69	-3326.06	5294.98	-4624.22	2365.60	-666.77	80.24	0.02	1.00
В-	0.69	-22.70	158.60	-444.77	337.84	1367.50	-4660.33	6928.94	-5944.45	3034.29	-858.72	104.04	0.02	1.00
AB-	1.00	-31.72	265.72	-1111.45	3026.68	-5888.34	8412.92	-8721.22	6308.82	-2985.03	823.32	-99.84	0.02	1.00
0	0.70	-30.79	267.40	-1244.76	3778.37	-7819.02	11204.45	-11101.60	7451.50	-3227.99	813.01	-90.31	0.02	1.00
A	0.80	-30.98	258.84	-1114.81	3089.65	-5864.52	7812.17	-7320.72	4729.14	-2002.04	498.72	-55.28	0.02	1.00
В	0.73	-29.21	240.94	-1023.39	2783.09	-5138.76	6602.71	-5932.42	3664.32	-1483.39	354.06	-37.71	0.02	1.00
AB	0.97	-34.90	296.77	-1305.54	3786.92	-7756.27	11379.64	-11815.02	8411.80	-3881.36	1040.61	-122.68	0.03	1.00
Rh+	0.75	-35.23	324.51	-1640.67	5452.40	-12326.34	19131.53	-20301.92	14431.88	-6556.91	1718.34	-197.40	0.03	1.00
Rh-	0.82	-26.84	201.51	-688.00	1259.03	-1021.13	-461.67	1981.83	-2113.07	1167.17	-340.22	41.52	0.02	1.00

In Graphs 2-9 of the temporal evolutions, statistical instabilities occur in the initial periods of analysis, as the number of deaths is reduced, and in the final periods they occur due to have few exposed countries for 166 days. The temporal evolution has smooth growth curves as shown in Graphs 2, 4, 6, and 8 of the correlations referring to Analyses 1-4, respectively. Graphs 3, 5 and 7, referring to the p-values, show that the acceptance of the correlations occurred right at the beginning of the time

series, in Graph 9, referring to the countries most affected (Analysis 4), the correlations were accepted between 51th and 80th days of exposure since the fifth death.

The results presented are sensitive to the population of each country, the more accurate it is, better results are obtained.





Graph 2 – Analysis of the ABO and Rh blood group and deaths from COVID-19 pandemic for 88 countries, using Pearson's correlation coefficient.

In Graph 2 (a) the temporal evolutions show that the correlations of blood type A+ have advantages in relation to other blood types and are immediately greater than those of the blood type O+. In 2 (b) referring to the ABO- blood group correlations, the pandemic progresses had a clear change causing the blood type O- to have a greater correlation than blood type A- after 73rd day. In 2 (c) when Rh factor is not distinguished, blood group O correlations were slightly higher than those of the A blood group after 92nd day. In 2 (d) regarding the Rh Factors, it is highlighted that blood type Rh- has greater correlations than those of the blood type Rh+ throughout the 166-day period.



Graph 3 – Analysis of p-values for Pearson's correlation coefficients for 88 countries.In Graph 3, the p-values reach values less than 0.05 at the beginning of the analysis, at the end of the study period there are fluctuations that can be justified by the scarcity of exposed countries.

Analysis 2: Temporal evolutions without outliers - the populous countries China and India

The curves shown in Graph 4 have a decreasing growth rate that tends to stabilize the same way as in Graph 2; it is also noticed that the temporal evolutions of the correlations of these two graphs were similar. This fact shows that the logarithmic transformations acted in order to standardize the data and to decrease the influence of the large populations of China and India.



Graph 4 – Analysis of the ABO and Rh blood group and deaths from COVID-19 pandemic, without the countries China and India, using Pearson's correlation coefficient.

In Graph 4 (d) as well as in 2 (d) of Rh factors, the correlations of the Rh-negative remained greater than those of the Rh-positive throughout the 166-day period.

Graph 5 of the p-values shows that the correlations are accepted at the first days of the period with 95% confidence and there were fluctuations both at the beginning period and at the end.



Graph 5 – Analysis of p-values for Pearson's correlation coefficients, without China and India.

The ABO/Rh-negative blood group in Graph 5 (b) was accepted before ABO/Rh-positive, and this also is observed in Graph 5 (d). These facts were seen in Graph 3 in similar behavior of the p-values' temporal evolutions.

Analysis 3: Temporal evolutions - least exposed countries

Graph 6 (b) highlights the maximum moderate correlations for blood types A- (ρ = 0.66), O- (ρ = 62), B- (ρ = 0.51) and AB- (ρ = 0.60) with p-values 0.00, analyzing the interval [35,120], these correlations were greater than those presented in Graphs 6 (a) and 6 (c) referring to the ABO and ABO(Rh+) blood groups.



Graph 6 – Analysis of the ABO and Rh blood and deaths from COVID-19 pandemic using Pearson's correlation coefficient, without China, India and extremely exposed countries.

Graph 6 (d) shows Rh-negative with maximum moderate correlation ($\rho = 0.63$) and weak for Rh-positive ($\rho = 0.33$). The correlations of the Rh- factors were greater than those of the Rh+ factor during

most of the study period. Graph 6 shows that when removing countries: Belgium, Brazil, France, Italy, Mexico, Spain, United Kingdom and USA, we do not observe important differences in the correlations.

In Graph 7 (a), 7 (c) and 7 (d) the p-values decreased slowly, in 7 (a) and 7 (c) for blood groups A+ and A, respectively, the correlations were accepted before than those of other blood groups. Graphs 7 (b) and 7 (d) show that the correlations of blood types with Rh- factor stands out with the acceptance in a shorter period than the other types analyzed.



Graph 7 – Analysis of p-values for Pearson's correlation coefficients, without China, India and extremely exposed countries.

The p-values' temporal evolutions behavior was similar for all Analyses (1-4), in Graph 9 (b) for ABO negative blood group was accept before ABO positive, this also is observed in Graph 9 (d).

Analysis 4: Temporal evolutions for extremely exposed countries

Graph 8 shows very strong maximum correlations for all blood groups and with smooth growth. Graph 8 (d) presents the maximum correlations for blood type Rh+ (ρ = 0.99, p-value = 0.00, CI = [0.77 0.99]) and Rh- (ρ = 0.95, p-value = 0.00, CI = [0.16 0.96]), all the maximum correlations obtained can be seen in Table 2.

Even though it is not statistically relevant due to the p-values, it is worth mentioning that in 8 (a)-(c) the AB blood group had greater correlations during most of the period analyzed followed by blood groups A, B and O. In Graph 8 (d) there is a clear parallelism between the temporal evolution of the Rh+ and Rh- blood groups.



Graph 8 – Analysis of the ABO and Rh blood group and deaths from COVID-19 pandemic using Pearson's correlation coefficient for extremely exposed countries.

Through the p-values in Graph 9, correlations are accepted between 50 and 100 days since the fifth death. Graphs 8 and 9 show a pandemic with wide variations in the correlation coefficients and p-

values for the first few days, suggesting the need for an analysis of the pandemic's behavior in relation to the number of daily deaths that is shown in the next topic.



Graph 9 – Analysis of p-values for Pearson correlation coefficients for extremely exposed countries.

Establishment rates of the COVID-19 pandemic

Graph 10 shows the pandemic visualization for Analyses 1-4 through the numbers of daily deaths. In this graph, for all analyses there is a common period at beginning of pandemic establishment between the 1st and 35th day, therefore independently of countries sets this period suggests defining virus expansion through populations. After that is shown for all analyses a period of stability that corresponds in the graph of the correlations to the period of smooth growth, finally in the last period the number of countries decrease escaped consequently the number of deaths and the correlation and pvalue curves fluctuate. It is also noticed when the stability period starts around the 35th day, the correlation graphs approach the inflection point.

Graph 11 shows in detail the period of establishment of the pandemic for the sets of considered countries, there is also a red line referring to the initial growth of the pandemic, between 14th and 35th day, using the least squares method.



Graph 10 – Number of daily deaths, since the fifth
death, for Analyses 1, 2, 3 and 4.Graph 11 – Number of daily deaths in detail considering
the first fifty days, for Analyses 1, 2, 3 and 4.

Table 7 defines the pandemic establishment rate for each of the analyses, and the relative values to Analysis 3, which corresponds to the least affected countries. Analysis 3 has lowest initial death rate (43 deaths per day), while Analysis 4, which refers to the set of countries most affected, a rate 5.6 times higher (242 deaths per day) is observed. Analysis 1 (88 countries) and Analysis 2 (88 countries except China and India) had relative rates of 6.75 and 6.65, respectively. Analyzed sets have the same growth period between the 14th and 35th day since the fifth death.

Table 7 – Pandemic establishment rate between the 14th and 35th day, calculated using the least squares method for the four sets of countries.

Analyses		Pandemic Estal (deaths p	olishment Rate per day)
	Rate	Std. Error	Rate / (Analysis 3 Rate)
1	289	19.35	6.75
2	285	19.07	6.65
3	43	3.43	1
4	242	17.64	5.6

Temporal Relationships of Rh blood groups

Graph 8 shows points of minimum correlation in items (a), (b), (c), and (d) for all blood groups analyzed, with a minimum point in 14 days from the fifth death. Correlations with p-values less than 0.05, were all accepted between 50 and 100 days. The correlations of the blood type Rh- are accepted with a lag of 14 days in relation to the blood type Rh+.

Graphs 8 (d) and 9 (d) show a 14-day lag-time between Rh blood groups. As can be seen in Graph 12 and detailed for the first fifty days in Graph 13, the blood type Rh+ is also shown, by way of comparison, with a 14-day lag; it is possible to notice a great similarity between the Rh blood groups correlations and p-values.

In Graph 12, the daily death rate curve shown in Graph 11 (d) is added. Note that the 14-day mark represents the beginning of the expansion phase of the pandemic with a growth rate significantly higher than the previous period (1st to 13th day), and has points of minimum correlation and minimum p-value for both blood types Rh+ and Rh-.



Graph 12 – *Comparative analysis between death rate, statistics (p-values and correlation coefficients)* show a 14-day lag-time between blood types Rh+ and Rh-, considering data logarithmic transformations.



Graph 13 – Detail for comparative analysis between death rate, *p*-values and correlation coefficients show a 14-day lag-time between Rh+ blood type and Rh-, considering data logarithmic transformations.

DATA ANALYSIS

Graph 14 shows the data normality tests from the logarithmic transformations which are accepted for Analysis 1-3. In this test, if p-value is greater than 0.5 the normality of the data is accepted. Analysis 4 has a small sample, so the normality test is statistically impaired, although it is a representative sample as to the number of deaths and rate, see Table 1 and Table 7.



Graph 14 – *Normality test for Analyses* 1 (*a*), 2 (*b*), 3 (*c*) and 4 (*d*).

Graph 15 refers to the number of deaths, on the *y*-axis, to the number of individuals with the blood types of each country, on the *x*-axis, uses logarithmic transformations of the data for the 120th day since the fifth death, referring from Analysis 1 with the 88 countries, in this example is presented the linear distribution of the data.



Graph 15 – Logarithmic transformations for deaths from COVID-19 and blood types, Analysis 1 on the 120th day since the fifth death.

In general, Graph 15 shows a linear behavior of the data, specifically blood types AB- and B- have greater linearity than AB+ and B+.



For all other analyses, a similar behavior is seen as in Graph 15, where only the number of analyzed countries changes.

Graph 16 – Deaths from COVID-19 and blood types, Analysis 1 in the 120th day.

Graph 16 shows the data without logarithmic transformations, in Graph 15 the same data are presented with the logarithmic transformations and the linear behavior is observed. In addition, the logarithmic transformation added a certain normality to the data, allowing the use of parametric statistics (Pearson).

Graph 17 shows data from the 120th day since the fifth death is presented for Analysis 1, in a global analysis of the number of deaths, with logarithmic transformations and sort them in increasing order by countries and the respective numbers of blood types.



Graph 17 – Logarithmic transformations of the ordered data (y-axis) and respective index referring to the country (x-axis), Analysis 1 was considered on the 120th day.

Analyses 2-4 have similar behaviors as seen in Graph 17, as only the number of analyzed countries changes. Table 8 shows the angular (a) and linear (b) coefficients, obtained by the least squares method,

with the respective associated errors, calculated for Analysis i (i = 1, 2, 3, 4) for the 120th day since the fifth death.

The data logarithmic transformation implies in a time-dependent linearization (t-days since the fifth death) given by:

$$y(t,x) = c(t) * e^{a(t)x}, ln(y) = b + a*x, b = ln(c),$$

where *x* refers to the index of each country in the ordered vector of blood types and number of deaths at time *t*, *y* (*t*, *x*) to the number of individuals with the respective blood types and number of deaths, a(t) to angular coefficient and b(t) refers to the linear coefficient.

Table 8 – Angular $(a_i(t))$, linear $(b_i(t))$, standard deviation and determination coefficients for Analyses i (i = 1, 2, 3, 4) for blood types and deaths from COVID-19, 120th day since the fifth death.

			Coe	fficients: A	Angular (a	_i) and Lin	ear (b _i)			
	Рор	A+	0+	B +	AB+	A-	0-	В-	AB-	Deaths
a_1	0.07	0.07	0.07	0.08	0.08	0.07	0.07	0.07	0.07	0.10
b_1	13.94	12.75	12.90	11.64	10.52	10.22	10.52	9.55	8.27	2.84
a_2	0.07	0.07	0.07	0.07	0.07	0.07	0.07	0.06	0.07	0.10
b_2	14.02	12.83	12.98	11.75	10.62	10.21	10.53	9.60	8.30	2.80
a_3	0.07	0.07	0.07	0.08	0.08	0.07	0.07	0.07	0.07	0.10
b_3	13.94	12.77	12.89	11.63	10.50	10.25	10.55	9.59	8.28	2.90
a_4	0.57	0.53	0.57	0.71	0.66	0.38	0.36	0.51	0.50	0.34
b_4	16.00	15.05	15.05	13.04	12.13	13.41	13.75	11.65	10.67	8.58
			Std erro	rs (<i>Err</i>) –	Coefficien	t of deterr	nination(<i>I</i>	R ²)		

	Po	р	Α	.+	0	+	В	+	A	B +	A	-	C)-	E	8-	AI	3-	Dea	ths
	Err	R^2	Err	R^2	Err	R^2	Err	R^2	Err	R^2	Err	R^2								
a_1	0.00	0.05	0.00	0.05	0.00	0.06	0.00	0.02	0.00	0.02	0.00	0.07	0.00	0.07	0.00	0.02	0.00	0.05	0.00	0.00
b_1	0.08	0.95	0.08	0.95	0.07	0.96	0.11	0.95	0.11	0.95	0.07	0.97	0.06	0.97	0.10	0.95	0.08	0.95	0.07	0.90
a_2	0.00	0.07	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.07	0.00	0.04	0.00	0.00	0.00	0.98
b_2	0.06	0.97	0.06	0.97	0.05	0.98	0.08	0.96	0.08	0.96	0.07	0.96	0.06	0.97	0.08	0.94	0.07	0.96	0.08	
a_3	0.00	0.07	0.00	0.07	0.00	0.00	0.00	0.04	0.00	0.04	0.00	0.07	0.00	0.00	0.00	0.00	0.00	0.05	0.00	0.98
b_3	0.06	0.97	0.07	0.97	0.05	0.98	0.10	0.94	0.10	0.94	0.07	0.97	0.06	0.96	0.10	0.92	0.08	0.95	0.07	
a_4	0.05	0.00	0.04	0.00	0.04	0.00	0.08	0.00	0.08	0.00	0.04	0.01	0.06	0.00	0.06	0.00	0.04	0.07	0.05	0.87
b_4	0.26	0.90	0.21	0.89	0.24	0.90	0.46	0.92	0.44	0.88	0.20	0.81	0.34	0.90	0.33	0.92	0.22	0.97	0.26	

In Table 8, the angular coefficients (a) referring to Analyses 1, 2 and 3 for blood groups ABO and Rh are very similar with a maximum difference of 0.01. For Analysis 4 the angular coefficient of the number of deaths from COVID-19 is approximately three times ($a_4 = 3.4$) higher than those of other analyses. The determination coefficients, with values equal or grater than 0.9 for Analyses 1, 2 and 3

and equal or greater than 0.81 for Analysis 4 demonstrate the quality of the polynomials in representing the point data.

An overview of the pandemic is obtained calculating the coefficients with an ordered vector, referring to the number of deaths, as shown in Table 8. This suggests a study in relation to time, so calculating the coefficients a and b that are dependent on time imply a way of characterizing the pandemic through the number of deaths. Graph 18 shows the time evolution of the angular (a (t)) and linear (b (t)) coefficients for Analyses 1 and 4.



Graph 18 – Angular and linear pandemic characterization coefficients for Analyses 1 and 4.

In Graph 18, the pandemic is characterized from Analysis 1 where a sample of 88 countries is analyzed. The studies in Analysis 4, on the other hand, show a particular characterization for the set of countries most exposed. Degree 7 polynomials were defined through the least squares method. The polynomial coefficients were well adjusted, since the values of the determination coefficients (R^2) are greater than 0.96 in all Analyses, as shown in Table 9.

Table 9 – Degree 7 polynomials coefficients of the temporal evolutions, where angular $(a_i(t))$ and linear $(b_i(t))$ coefficients are obtained by the method of least squares, standard deviation of the residue (DesvErr) and determination coefficient (R^2) for Analyses i = 1, 2, 3 and 4.

			Pa	andemic	Charae	cterizatio	on			
	Intercept	I_1	I_2	I_3	I_4	I_5	I_6	I 7	DesErr	R^2
a_1	0.00	0.50	-1.71	4.52	-8.22	8.85	-4.93	1.09	0.00	1.00
b_1	1.43	0.40	19.20	-88.00	181.03	-187.64	94.52	-18.21	0.05	0.99
a_2	0.00	0.51	-1.81	4.92	-9.07	9.79	-5.45	1.20	0.00	1.00
b_2	1.43	0.27	19.57	-89.68	185.22	-192.78	97.53	-18.89	0.06	0.99
<i>a</i> ₃	0.00	0.52	-2.20	6.33	-11.41	11.86	-6.38	1.37	0.00	1.00
b_3	1.43	-0.17	30.12	-127.36	247.41	-247.55	122.38	-23.45	0.06	0.99
a_4	0.03	3.60	-16.47	38.23	-51.36	40.06	-16.69	2.86	0.01	0.96
b_4	1.26	20.88	30.13	-217.24	408.24	-371.81	167.95	-30.11	0.06	1.00

DISCUSSION and CONCLUSION

Zhao [1] associated A blood group with a higher risk of contamination and death by COVID-19, when compared to the non-A blood groups and lower O blood group when compared to non-O groups. Zietz [2] and Latz [3] concluded that A blood group was more likely to contract the virus than O blood group, but without evidence of associations for serious cases or deaths. Arac [11] in clinical studies for the period from 16 March to 20 May, 2020, suggests that the blood type Rh+ is predisposed and Rh-has some protection for COVID-19.

The epidemiological approach used here was to analyze the Pearson's correlations between blood groups (ABO and Rh), distributed in 88 countries, and cumulative number of deaths due to COVID-19. Significant correlations were observed for Rh blood group, which suggest an important role in the evolution of the pandemic, mainly for blood types A- and O-. The p-values showed that the correlations for Analyses 1 (set of 88 countries), 2 (set of countries except China and India) and 3 (set of least exposed countries), regardless of blood group, were accepted at the beginning of the time evolution. When applying the logarithmic transformations to the data, less variability is perceived therefore the

acceptations of the correlations through the p-values occur already in the initial periods of the pandemic.

Comparing Analyses 1-2 with Analysis 3, it is clear that when countries with a high number of deaths are removed, the correlations are reduced. This fact combined with the greater correlation between blood groups (ABO, ABO+, ABO- and Rh) and the number of deaths obtained in Analysis 4 (extremely exposed countries) could suggest a social action on the pandemic related to the associated biological factors (blood groups), demanding less from the biological defense of each individual.

In all analyses, A blood group had greater correlations than O blood group in most of the analyzed period (166 days since the fifth death), for maximum correlations was obtained values of the confidence intervals greater than zero, except for AB blood group in Analysis 4. Analyses 1-3 presented blood types (A+, O+) with moderate maximum correlations and Analysis 4 were very strong maximum correlations, but are unreliable results due to the fact that confidence intervals are very wide and contains zeros.

Analysis 4 had the greatest correlations, although with a higher number of deaths statistically the results of the correlations were accepted only at the end of the analyzed period. In this temporal analysis there is a certain parallelism of the correlation coefficients, and for the Rh blood group correlations, blood type Rh- presents correlations that are 14 days out of step in relation to the blood type Rh+. Another fact is the occurrence of the growth of p-values in the period of highest death rate, considered between the 14th and 35th day since the fifth death, consequently non-acceptance of the correlations, which occurs after a certain stability of the death rates, suggesting that in an environment of accelerated contamination it is not possible to establish statistically acceptable correlations.

The relationship found between the Rh blood groups (Rh+ and Rh-) with the greatest correlations in the temporal Analyses 1-3 of the blood type Rh- suggests the need to proceed with studies in this direction. Clinical/Epidemiological studies have often failed to detect these relationships yet, possibly due to the following factors: scarce data for the blood type Rh-, approaches for short and geographically localized periods, but recent studies have already begun to draw attention to this approach.

Based on studies showing that blood type Rh-negative has a certain protection against viral attacks Flegr[15], the greatest correlations obtained here could suggest an important role of Rh-negative blood type in a broader scope of the virus spread.

In this approach, the temporal evolution of the correlation coefficients between the blood types of the ABO/Rh blood groups system, from four sets of analyzed countries is a dynamic process and

depends on the time of exposure to the virus SARS-CoV-2, which could be influenced by the social and biological factors that cover the pandemic, given the characteristics of each set. The social influence could be indicated newly when the pandemic establishment rate obtained for the set of countries most affected is 5.6 times greater than set least exposed. The pandemic establishment rate shows some dynamic of virus spread, for all sets of analyzed countries was found a common period at beginning of pandemic between 1st and about 35th day since the fifth death, therefore independently of country sets this characteristic period suggests to define the virus spread through the populations around the world. This fact explains the great importance of social factors in the early days of the pandemic.

When considering the cumulative data from 166 days since the fifth death, it was possible to make a comprehensive assessment and interpret the pandemic through the correlation coefficients modeled by polynomial parameters. Additionally, the parameters defined here for COVID-19 pandemic referring to the rate of establishment and the pandemic characterization coefficients parameters through the number of deaths might be useful for future comparisons.

The results presented here indicate the need for complementary clinical and epidemiological studies, which could contribute to the results obtained. This working team group has expanded the analysis period, then intends to search for open databases to apply other statistical techniques and data mining in order to deepen the epidemiological studies.

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Comments

In respect for the victims and their families, each one represented in these numbers was treated with the greatest sense of respect and dignity.

Conflict of interest

The authors declare that there are no conflicts of interest.

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REFERENCES

- [1] Zhao J, Yang Y, Huang H, Li D, et al. Relationship between the ABO Blood Group and the COVID-19 Susceptibility, medRxiv 2020.03.11.20031096.
 doi: <u>https://doi.org/10.1101/2020.03.11.20031096</u>
- [2] Zietz M, Zucker JE, Tatonetti NP. Testing the association between blood type and COVID-19 infection, intubation, and death, medRxiv 2020.04.08.20058073.
 doi: https://doi.org/10.1101/2020.04.08.20058073
- [3] Latz CA, DeCarlo C, Boitano L, *et al.* Blood type and outcomes in patients with COVID-19. *Ann Hematol*, 2020;99:2113–2118. doi: <u>https://doi.org/10.1007/s00277-020-04169-1</u>
- [4] Ellinghaus D, Degenhardt F, Bujanda LMD, *et al.* Genomewide Association Study of Severe COVID-19 with Respiratory Failure David Ellinghaus, The New England Journal of Medicine, 2020;383:1522-1534. doi: <u>https://doi.org/10.1056/NEJMoa2020283</u>
- [5] Alkout TA., Alkout AM. ABO blood groups among Coronavirus disease 2019 patients, Ibero American Journal Of Medicine, 2020;4:268-274.
 doi: <u>https://doi.org/10.5281/zenodo.3893256</u>.
- [6] Takagi H. Down the Rabbit-Hole of blood groups and COVID-19. British Journal of Haematology, 2020;190:268-288. doi: <u>https://doi.org/10.1111/bjh.17059</u>
- [7] Mourant AE, Kopec AC, Domaniewska-Sobczak K. Blood groups and diseases. A study of associations of diseases with blood groups and others polymorphisms. London: Oxford University Press, 1978; 328p.
- [8] Mattos LC de, Moreira HW. Genetic of the ABO blood system and its link with the immune system Rev. Bras. Hematol. Hemoter, 2004;26(1):60-63.
- [9] Cheng Y, Cheng G, Chui CH, et al. ABO Blood Group and Susceptibility to Severe Acute Respiratory Syndrome. *JAMA*, 2005;293(12):1447-1451.
 doi: https://doi.org/10.1001/jama.293.12.1450-c

- [10] Chen Y, Liu Q, Guo D. Emerging coronaviruses: Genome structure, replication, and pathogenesis.
 J Med Virol, 2020; 92(4):418-423. Epub 2020 Feb 7. Erratum in: J Med Virol, 2020 Aug2; PMID: 31967327; PMCID: PMC7167049. doi: <u>https://doi.org/10.1002/jmv.25681</u>
- [11] Arac E, Solmaz I, Akkoc H, et al. Association Between the Rh Blood Group and the COVID-19 Susceptibility, International Journal of Hematology and Oncology, 2020;30(2): 81-86. doi: <u>https://doi.org/10.4999/uhod.204247</u>
- [12] Feng C, Wang H, Naiji LU, Chen T, et al. Log-transformation and its implications for data analysis, Shanghai Arch Psychiatry, 2014;26(2):105-109.
 doi: <u>https://dx.doi.org/10.3969/j.issn.1002-0829.2014.02.009</u>
- [13] MacQueen JB. Some Methods for classification and Analysis of Multivariate Observations. Proceedings of 5th Berkeley Symposium on Mathematical Statistics and Probability. University of California Press, 1967;281-297.
- [14] Kim J, Bang H. Three common misuses of P values, Dent Hypotheses, 2016;7(3):73-80.doi: <u>https://doi.org/10.4103/2155-8213.190481</u>
- [15] Flegr J, Hoffmann R, Dammann M, Worse Health Status and Higher Incidence of Health Disorders in Rhesus Negative Subjects. PLOS ONE, 2015;10(10):e0141362. doi: <u>https://doi.org/10.1371/journal.pone.0141362</u>

APPENDIX

Table 10 – Populations and percentage of ABO and Rh blood groups for the set of 88 countries.

	l percentage	of ABO	ana Rh b	looa gro	ups for ti	ne set of	88 counti	ries.	
gentina	Pop. 44270440	0+ 0.454	A+ 0.343	B+ 0.086	AB+ 0.026	0- 0.084	A- 0.004	B- 0.002	AB- 0.001
nenia	2931568	0.290	0.463	0.120	0.056	0.020	0.037	0.010	0.004
stralla	24642693 8592470	0.400	0.310	0.080	0.020	0.090	0.070	0.020	0.010
nrain	1418695	0.485	0.193	0.226	0.037	0.033	0.013	0.010	0.003
ngladesh	164833667	0.312	0.214	0.346	0.089	0.014	0.010	0.010	0.006
gium livio	10414336	0.380	0.340	0.085	0.041	0.070	0.060	0.015	0.008
snia and Herzegovina	3792730	0.310	0.294	0.101	0.011	0.044	0.027	0.005	0.001
zil	211248418	0.360	0.340	0.080	0.025	0.090	0.080	0.020	0.005
Igaria	7045097	0.280	0.370	0.130	0.070	0.050	0.070	0.020	0.010
meroon nada	24515533	0.428	0.388	0.120	0.033	0.014	0.012	0.004	0.001
ile	18314060	0.855	0.087	0.034	0.010	0.012	0.001	0.001	0.001
ina	1388251023	0.477	0.278	0.189	0.050	0.003	0.002	0.001	0.000
lombia	49069267	0.613	0.261	0.023	0.015	0.051	0.027	0.007	0.003
oatia ha	4207355	0.290	0.360	0.150	0.050	0.050	0.060	0.030	0.010
nmark	5711902	0.350	0.335	0.080	0.029	0.060	0.028	0.020	0.010
minican Republic	10766932	0.462	0.264	0.169	0.031	0.037	0.021	0.014	0.002
uador	16665756	0.750	0.140	0.071	0.005	0.024	0.007	0.003	0.000
ypt Ionia	95220838 1305745	0.520	0.240	0.124	0.038	0.050	0.020	0.006	0.002
niopia	104352727	0.390	0.280	0.210	0.050	0.043	0.045	0.010	0.010
land	5541328	0.270	0.380	0.150	0.070	0.040	0.060	0.020	0.010
ince	64939560	0.360	0.370	0.090	0.030	0.060	0.070	0.010	0.010
rmany	80635980	0.350	0.370	0.090	0.040	0.060	0.060	0.020	0.010
inea	13291741	0.469	0.216	0.229	0.037	0.020	0.009	0.020	0.002
nduras	9348898	0.575	0.270	0.078	0.025	0.027	0.017	0.006	0.002
ngary	9787801	0.270	0.330	0.160	0.080	0.050	0.070	0.030	0.010
land lia	334311	0.476	0.264	0.093	0.016	0.084	0.046	0.017	0.004
lonesia	263519317	0.368	0.259	0.288	0.089	0.002	0.000	0.002	0.000
7	80982137	0.335	0.270	0.222	0.070	0.040	0.030	0.025	0.008
7	38657787	0.321	0.250	0.256	0.074	0.036	0.027	0.027	0.009
and	4749263	0.470	0.260	0.090	0.020	0.080	0.050	0.020	0.010
V	59797969	0.320	0.360	0.075	0.025	0.030	0.040	0.020	0.005
naica	2813316	0.470	0.230	0.200	0.030	0.035	0.020	0.010	0.005
pan	126044340	0.299	0.398	0.199	0.099	0.002	0.002	0.001	0.001
nya	48470780	0.456	0.252	0.213	0.042	0.018	0.010	0.009	0.000
Via	1944122	0.306	0.310	0.170	0.060	0.054	0.060	0.030	0.010
iva	6408990	0.426	0.289	0.112	0.045	0.063	0.042	0.016	0.007
huania	2827573	0.360	0.330	0.110	0.040	0.070	0.060	0.020	0.010
xembourg	587297	0.350	0.370	0.090	0.040	0.060	0.060	0.020	0.010
cedonia Iaveia	2083690	0.300	0.340	0.150	0.060	0.050	0.060	0.030	0.010
uritania	4266765	0.463	0.267	0.175	0.038	0.028	0.016	0.001	0.002
uritius	1267303	0.383	0.260	0.250	0.067	0.017	0.010	0.010	0.003
xico	130227836	0.558	0.299	0.080	0.016	0.027	0.015	0.004	0.001
anmar	53507932	0.357	0.238	0.327	0.069	0.003	0.002	0.003	0.001
bai therlands	17033012	0.352	0.283	0.271	0.086	0.003	0.002	0.002	0.001
v Zealand	4604996	0.380	0.320	0.090	0.030	0.090	0.060	0.020	0.010
geria	191851411	0.513	0.224	0.207	0.026	0.016	0.007	0.006	0.001
rway kistan	5330986	0.330	0.415	0.068	0.034	0.060	0.075	0.012	0.006
การเสบา ru	32167717	0.246	0.206	0.344	0.095	0.042	0.027	0.036	0.004
ilippines	103801747	0.369	0.289	0.269	0.070	0.001	0.001	0.001	0.000
land	38563480	0.310	0.320	0.150	0.070	0.060	0.060	0.020	0.010
rtugal	10264672	0.363	0.400	0.066	0.029	0.060	0.066	0.011	0.005
mania	19237087	0.285	0.318	0.176	0.070	0.050	0.060	0.030	0.011
ssia	143374801	0.280	0.300	0.200	0.070	0.049	0.058	0.032	0.011
udi Arabia	32744532	0.478	0.239	0.170	0.040	0.040	0.020	0.010	0.003
rbia	8776827	0.319	0.353	0.126	0.042	0.061	0.067	0.024	0.008
ngapore wakia	5784819	0.436	0.239	0.244	0.060	0.009	0.007	0.004	0.001
venia	2071258	0.310	0.330	0.120	0.060	0.070	0.070	0.030	0.010
uth Africa	55437815	0.390	0.320	0.120	0.030	0.060	0.050	0.020	0.010
uth Korea	50748307	0.279	0.339	0.269	0.110	0.001	0.001	0.001	0.000
ain dan	46070163	0.360	0.340	0.080	0.025	0.090	0.080	0.020	0.005
eden	9920843	0.320	0.370	0.100	0.028	0.060	0.018	0.020	0.010
itzerland	8454321	0.350	0.400	0.070	0.030	0.060	0.070	0.010	0.010
ria	18920698	0.430	0.300	0.140	0.037	0.050	0.030	0.010	0.003
ailand	68298027	0.408	0.169	0.368	0.050	0.002	0.001	0.002	0.000
key anda	80420065 43276102	0.298	0.378 0.300	0.142	0.072	0.039	0.047	0.016	0.008
raine	44404078	0.320	0.340	0.150	0.050	0.050	0.060	0.020	0.010
ited Arab Emirates	3398017	0.441	0.219	0.209	0.043	0.043	0.021	0.020	0.004
ted Kingdom	65512375	0.370	0.350	0.080	0.030	0.070	0.070	0.020	0.010
ted States	326481533	0.374	0.357	0.085	0.034	0.066	0.063	0.015	0.006
tnam	95414640	0.417	0.233	0.308	0.010	0.003	0.001	0.002	0.002
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