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Original article

Genetic polymorphisms of blood donors in Algeria through blood groups ABO, RH, and Kell

Polymorphismes génétiques des donneurs de sang en Algérie à travers les groupes sanguins ABO, RH et Kell

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ABSTRACT

Our study included 2465 blood donors unrelated from both sexes, originating from Msila (Algeria), at Msila Blood Transfusion Center (CTS), with the aim of performing an anthropogenetic characterization of the population of M'sila, by studying the three-erythrocyte polymorphic systems ABO, Rhesus, and Kell with their allele frequencies. This allowed us to demonstrate after a multi-varied comparative analysis through principal components analysis (PCA) and hierarchical cluster analysis (HCA) On the one hand, comparing the population of Msila to the different regions of Algeria where we found a genetic proximity with the great south of Algeria going towards the south-east of Algeria. On the other hand, the comparative analysis of Msila's population with other populations in the world based on historical, geographical and cultural profile, by building a tri-hybrid potential parenting model (North Africa, Mediterranean and Middle orient) through the three blood systems, allowed us to identify four potential parents including Egypt and Libya (North Africa) and Saudi Arabia and South Yemen (Middle East), Regarding the third strand of our tri-hybrid model, we did not find any potential parental link with the northern shore of the Mediterranean (southern Europe) despite the historical and geographical link that exists. This study allowed us to share the map of Algeria genetically into two blocks: a North block and a South block. It also allowed us to trace a retrograde genetic route through the time of the M'sila population, thus determining these potential parental origins.

RÉSUMÉ

Mots clés :
Groupes sanguins
Fréquences génétiques
Population
Caractérisation
CAH et ACP

Notre étude a porté sur 2465 donneurs de sang des deux sexes non apparentés, et originaires de Msila (Algérie), au niveau de centre de transfusion sanguine de Msila (CTS), dans un but de réaliser une caractérisation anthropo-génétique de la population de Msila, en étudiant les trois systèmes polymorphes érythrocytaire ABO, Rhésus et Kell avec leurs fréquences allyliques. Ce qui nous a permis de démontrer après une analyse comparative multivariées à travers une ACP et une CAH. D'un coté, en comparant la population de Msila aux différentes régions de l'Algérie où on a trouvé une proximité génétique avec le Grand Sud algérien en allant vers le sud-est de l'Algérie. D'un autre coté, l'analyse comparative de la population de Msila avec des populations dans le monde à travers ces trois systèmes sanguins et leurs fréquences allyliques et basés sur le profil historique, géographique et culturel, en construisant un modèle parental potentiel tri-hybride (Nord Afrique, pourtour méditerranéen et Moyen Orient) ce qui nous a permis de déterminer quatre parents potentiels dont l'Egypte et la Lybie (Nord Afrique) et l'Arabie saoudite et Yémen-sud (Moyen Orient), par contre nous n'avons pas trouvé du lien parental potentiel avec

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la rive nord de la méditerranée (le sud de l'Europe) malgré le lien historique et géographique existant. Cette étude nous a permis de partager la carte de l'Algérie génétiquement en deux blocs : un bloc Nord et un Bloc sud. Elle nous a permis aussi de tracer un itinéraire génétique rétrograde à travers le temps de la population de Msila, en déterminant ainsi ces origines parental potentiels.

1. Introduction

Blood group systems were taken for a solid platform in most antropo-genetic and immuno-hematological studies of populations. By studying these biological markers, their frequencies, and their distributions we are able to characterize populations. In Algeria for over 70 years many studies have been conducted whose first study dates back to 1933 [1], but all of these studies have focused on small isolates or tribal groups however, Benabadji and Chamla [2] reinitialize genetic studies in this region, examining a large sample of Algerian blood donors for ABO; Rhesus. These studies were analyzed again by Lefevre-Witier et al. [3] because according to them the study of Benabadji and Chamla [2] was not conclusive enough. Our work comes under this theme, by studying a sample of 2465 blood donors at the Msila blood transfusion center (CTS). by integrating this sample of the M'sila population into the model of Lefevre-Witier et al. [3] in order to obtain an anthropogenetic characterization of Msila's population and to model again all the regions of Algeria, as well as to contribute to enrich the database of transfusion medicine whether from the regional or national point of view in order to well secure the transfusion act.

2. Overview of the story of M'sila

M'sila is located just 240 kilometers south-east of Algiers and is nestled on an altitude of 469 meters. This city, which is part of the highlands, forms a large depression in the heart of the country. Located at the outlet of the dam Ksob.

Many advanced civilizations have exploited this region for centuries, among others the Roman civilization after the fall of Carthage in the 2nd century BC Massinissa governs Numidia, country in the borders stretch from the Moulouya (west) to the Amsaga (in the East), with capital Cirta (Constantine); after him and despite Jugurtha's resistance to Roman pressure, in the 1st century of the Christian era, Emperor Caligula annexed the vast empire country of Rome [1]. More than five centuries of Roman presence have left the traces of a civilization whose vestiges dot, nowadays the territory. Debris of aqueducts and cisterns and even rock engravings. All these monuments attest to the passage of Roman warriors and merchants who had chosen Tobna, Magra and M'sila as governors' seats [1]. This civilization will not resist, however, the invasion of the Vandals in the 6th century. With the arrival of the Arabs, M'sila was created by Abul Kassem, the Fatimid dynasty in 927 [1].

Abu Corra, the Kharidjite caliph of Tlemcen (West Algeria), with 40,000 soldiers, besieged Tobna in 765, as well as the whole territory, to Herdada, which is now backed by Bousada. Hammad Ben Bouloughine will govern, from the eleventh century, the entire central Maghreb, from Achir, including the Hodna in 1007, North East of M'sila, he founded the citadel, El Kelâa in 1052. Beni Hillel (Southern Yemen) arrived, although having resisted the invasion; the Hammadids had to be pushed back to the West where they establish their new capital, in 1067. The expansionism of the Turks of the North towards the center of the country was concretized by the setting up military posts to end the insurgency and anarchy, with the help of some tribal leaders. M'sila which constituted an advanced post, presents some indicative revealing of this presence. The Turkish community lived in a district called Karghla which kept its name until its destruction by a violent earthquake in 1965 [1].

It was only eleven years after the invasion of the French Empire, in 1841, that it was occupied by the French army. It then had only 1,500 inhabitants, living from trade and agriculture. Shaved several times and rebuilt each time, it has a strong expansion towards the West, since the early 1970s, it is chief town of Wilaya in 1974, industrial city and university, M'sila is also a high place heritage thanks to its Kalâa.

3. Materials and methods

A retrospective analytical study of 2465 voluntary and healthy blood donors of both sexes, at Msila's blood transfusion center (CTS). The registers of (CTS) served as a support for the collection of information. Blood donors were collected in compliance with good sampling and asepsis practices; after an interview and a medical examination, a sample of 2465 blood donors unrelated and originating from Msila was selected. All blood samples collected from the blood donors of the M'sila population were tested for the three polymorphic erythrocyte systems: ABO, Rhesus, and Kell.

3.1. Phenotypic determination

The typing of ABO antigens, RH (C.D.E.c.e), and Kell was performed by agglutination tests on plate and gel card (BioRade) at room temperature, using two different sera for each antigen. Three blood systems and their alleles were subject to exploitation.

3.2. Data analysis

The estimation of the allele frequencies for ABO systems we have adopted the Bernstein [4] formula, while for the allelic frequencies RH was calculated from the observed phenotype frequencies by the Wiener [5] method based on Hardy Weinberg equilibrium assumptions using the R software Package [6]. The genetic distances were calculated on the basis of the allelic frequencies of the three blood systems studied ABO, RH, and Kell using the Reynolds method [7] and the R software Package [6].

3.3. Intra and inter-population comparison

3.3.1. Intra-population comparison

In order to establish an observable model of genetic and geographical variation Lefevre-Witier et al. [3] re-analyzed the data of Aireche [8] and compiled the total sample of Algeria in ten regions, based on ecology, history, and geography. This subdivision into ten regions (Fig. 1) includes a set of wilayas (the basic administrative units of Algeria), these areas are spread from west to east Algeria. To establish a genetic affinity between the different regions of Algeria and the population of Msila supposed to be contributing to the genetic mixture of the entire Algerian territory based on cultural, historical and geographical data, a multidimensional analytical vision was adopted, using the principal component analysis (PCA), and in order to visualize this genetic affinity between the population of Msila and the ten regions, an illustrative model has

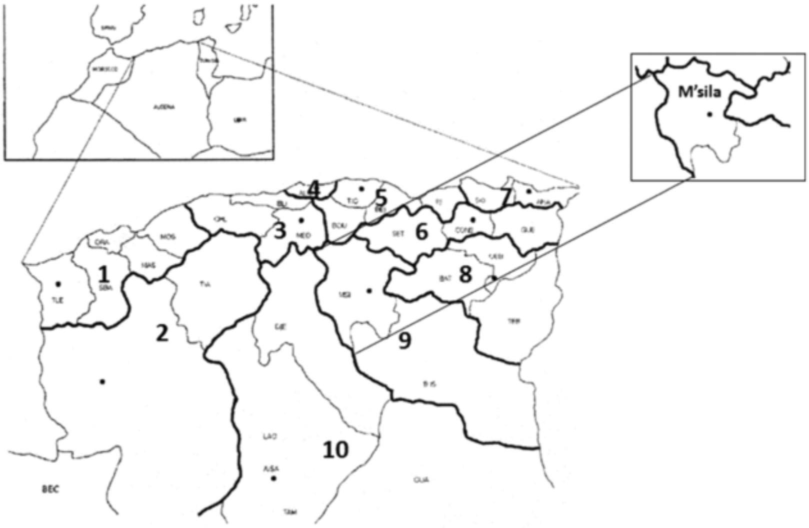

Fig. 1. The geographical locations of Msila and the ten regions of Algeria according to Lefevre-Witier et al. [3].

been adopted, using as an illustrative individual the total of Algeria [9] in this (PCA). The second method of analysis called hierarchical cluster analysis (HCA) allows us to group together whole regions of the country in a homogeneous class this allows us to deduce genetic affinity relationships between different regions by constructing a dendrogram hierarchy using genetic distances.

3.3.2. Inter-population comparison

To genetically characterize the population of Msila worldwide, we have chosen for a tri-hybrid model for the admixture analysis, by using three potential parental populations (North Africa, Middle East, and the shore of the Mediterranean) we assume that there is an equal contribution of these three parent populations. Populations selected for inter-population comparison are selected from the literature and shown in Table 1. These comparisons between the Msila population and the other populations of the tri-hybrid model were evaluated by a varied multi-analysis, using (PCA), and in order to have a rather fine vision of the genetic relations of the populations compared with that of Msila. We have also adopted a hierarchical cluster analysis (HCA).

4. Results and discussion

4.1. Intra-population comparison

Table 1 groups the phenotypic frequencies distribution and the allele frequencies obtained for the three systems ABO, RH, and Kell. Hardy Weinberg equilibrium was confirmed by a Chi^2 at a level of 5%. For the ABO system, we find a predominance of the O phenotype (57.28%) followed by group A (24.83%) then B (12.41%) and

Table 1
Observed phenotypes and estimated Allele frequencies of Msila population.

System	Phenotype	Observed frequency (%)	Allele	Estimated Allele frequency (%)
ABO (n = 2465)				
	A	24.83 (n = 612)	A	16.45
	B	12.41 (n = 306)	B	9.34
	O	57.28 (n = 1412)	O	74.59
	AB	5.48 (n = 135)		
RH (n = 2465)				
	Dccee	15.21 (n = 375)	DCe (R_1)	37.25
	DccEe	9.45 (n = 233)	DcE (R_2)	12.08
	DccEE	1.95 (n = 48)	Dce (R_0)	21.15
	DCcee	41.05 (n = 1012)	dce (r)	25.40
	DCcEe	9.37 (n = 231)	dCe (r_1)	2.01
	DCcEE	0.04 (n = 1)		
	DCCee	15.38 (n = 376)		
	DCCEe	0.20 (n = 5)		
	dccee	6.45 (n = 159)		
	dccEe	0.20 (n = 5)		
	dccEE	0.04 (n = 1)		
	dCcee	0.57 (n = 14)		
	dCcEe	0.04 (n = 1)		
	dCCee	0.04 (n = 1)		
Kell (n = 2465)				
	KK	–	K	4.08
	Kk	7.99 (n = 197)	K	95.92
	kk	92.01 (n = 2268)		

Table 2
Gene frequencies of Msila population's and the ten regions of Algeria.

Region	ABO*A	ABO*B	ABO*O	RH*R_1	RH*R_2	RH*R0	RH*r	RH*r_1	K	References
Msila	0.1645	0.0934	0.7459	0.3725	0.12	0.2115	0.254	0.0201	0.0408	This work
Region 1	0.1883	0.1222	0.6895	0.3814	0.0912	0.2331	0.2784	0.0132	0.0461	[a]
Region 2	0.196	0.1429	0.6611	0.3874	0.0836	0.2377	0.2688	0.0076	0.0528	[a]
Region 3	0.251	0.1176	0.6314	0.3933	0.0917	0.2533	0.2397	0.0137	0.0482	[a]
Region 4	0.2165	0.1273	0.6561	0.4385	0.074	0.1975	0.2594	0	0.0414	[a]
Region 5	0.2222	0.1269	0.6509	0.4373	0.0746	0.1964	0.2768	0.0071	0.0523	[a]
Region 6	0.1957	0.1243	0.68	0.4251	0.0963	0.2256	0.22	0.0305	0.0556	[a]
Region 7	0.2276	0.1326	0.6398	0.4522	0.0832	0.1962	0.2504	0.0153	0.0475	[a]
Region 8	0.2098	0.1166	0.6737	0.4378	0.1064	0.2375	0.1758	0.0426	0.0376	[a]
Region 9	0.1984	0.1111	0.6905	0.4115	0.1057	0.1908	0.2386	0.0334	0.0616	[a]
Region 10	0.1373	0.1373	0.7255	0.3592	0.1499	0.2828	0.2082	0	0.0338	[a]
Algeria totale	0.2093	0.123	0.6677	0.42371	0.0766	0.209	0.28661	0.00281	0.049	[b]

[a] Lefevre-Witier et al. [3].
[b] Aireche and Benabadji [9].

finally AB (5.48%). The most dominant allele frequencies are ABO*O (74.59%), followed by ABO*A (16.45%) and ABO*B (9.34%). For the rhesus system in our population, the most common RH haplotype is R_1 (37.24%) followed by haplotype r (25.40%), R_0 (21.15%). These four haplotypes R_1 (DCe), r (dce), R_0 (Dce) and R_2 (DcE) are the most common haplotypes in the Msila population. For the typing of the Kell system, we have a low frequency of the K allele (4.08%). For comparison, we are also presented the gene frequencies of Msila population's and the ten regions of Algeria in Table 2. The genetic distances between the population of Msila and the different regions of Algeria used for comparison are presented in Table 3. The comparison of distances chosen in ascending order makes it possible to share Algeria in two categories compared to the population of Msila and according to the genetic distance: Category I whose distance less than 0.1 groups the two regions; the west of Algeria (region 1) which includes 5 wilayas, and the Algerian center going to the Algerian south-east (region 9). Category II with distances greater than 0.1 which includes the eight remaining regions of Algeria (region 2, region 3, region 4, region 5, region 6, region 7, region 8, region 10). The lowest genetic distance is found with Region 1 (0.0811) and the furthest distance from Msila is Region 7 (0.157) that of North East of Algeria (Annaba and Skikda) which allows us to find a significant proximity between the population of Msila and the west of Algeria and the center of the country, going to the south-east, however the population of Msila is very far from the North East of Algeria (Annaba and Skikda) followed by the center by going towards the south west of Algeria, this is consistent with Msila's historical as well as the historical migratory flow of the city of Msila. A multidimensional analysis in the form of PCA of our eleven Algerian populations is shown in (Fig. 2). This analysis shows an overall variability of 69.28% of which (50.42%) for the first dimension and (18.86%) for the second dimension. The R_2 haplotype and the O allele are strongly negatively correlated with the first dimension and the populations with a high frequency of these alleles are

Table 3
Genetic distances between the population of Msila and the different regions of Algeria.

Population	Reynolds distance
Msila	0.0000
Region 1	0.0811
Region 9	0.0858
Region 6	0.1057
Region 10	0.1067
Region 2	0.1150
Algeria total	0.1210
Region 4	0.1364
Region 8	0.1380
Region 5	0.1436
Region 3	0.1563
Region 7	0.1574

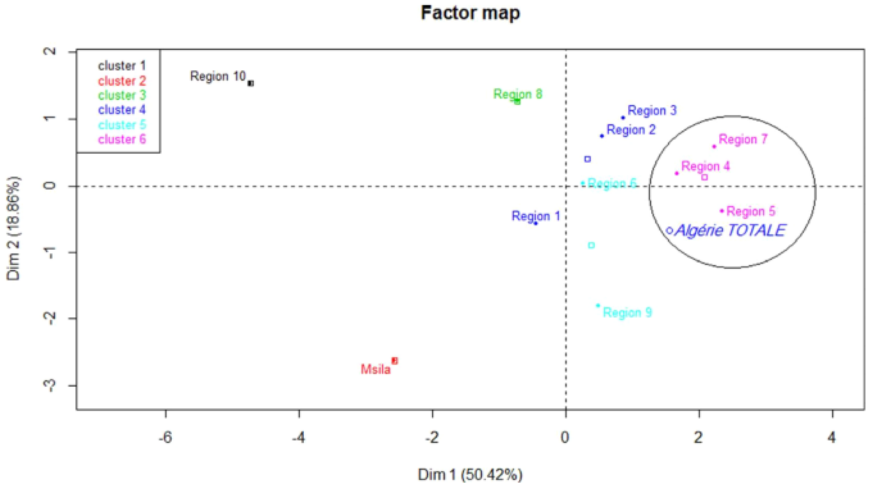

Fig. 2. Principal components analysis for Msila population's and the ten regions of Algeria tested for ABO, RH and KEL.

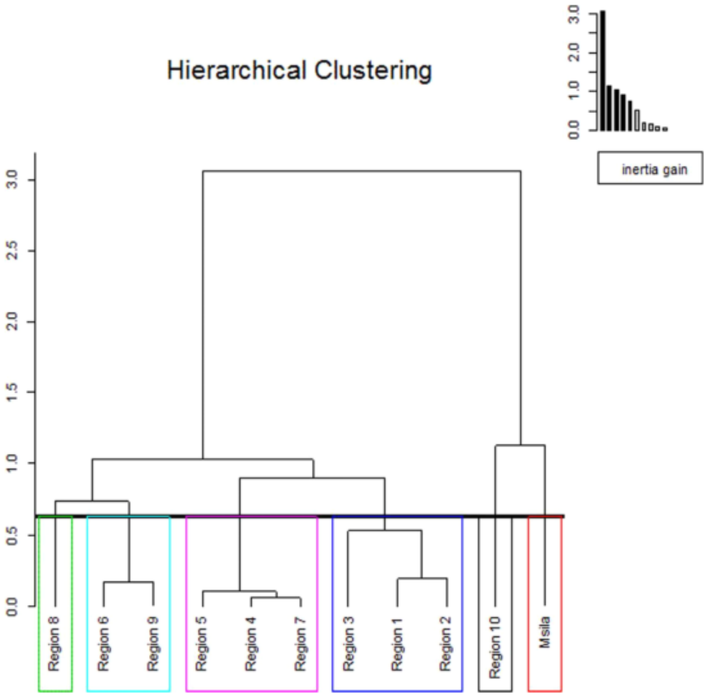

Fig. 3. The hierarchical cluster analysis for Msila population's and the ten regions of Algeria tested for ABO, RH and KEL.

positioned in the same direction on the left (Our population and the region 10: southern of Algeria). The A allele and the R_1 haplotype are strongly positively correlated with the first dimension and the populations with a high frequency of these alleles are positioned in the same direction on the right (North-East of Algeria: Annaba and Skikda as well as the north-center of Algeria going from the center to the North East: Algiers, Bejaia, Tizi-Ouzou. . .). Compared with the second dimension of our P.C.A, the B allele is correlated, but the R_0 haplotype is partially correlated with this dimension, and the populations with a high frequency of these alleles are also positioned in the same direction to the right of the second Axis, the latter opposes the population of Msila and the region 9 which includes Msila to the south-east of Algeria with their low frequencies in the K allele and the haplotype r, to the populations of the north of Algeria, going from north to North East of the country.

If we take the total of Algeria [9] as an illustrative individual in this multidimensional model, we can clearly see that the population of Msila with the great south of Algeria (region 10) and the region 9 which includes Msila going south-east form a single block marked by the O allele, the R_2 haplotype, partially the R_0 haplotype, and the K allele compared to other regions of the northern of Algeria part which together with Algeria total make another block alone marked by the A allele, and the R_1 haplotype (see Fig. 2), which is in good agreement with the historical and cultural migratory flow of this country, because the region of Msila is considered geographically as the door of Algerian desert and so named as such up to this day, and the sense of the migratory flow Algerian which experienced its boom in early 1980 from south to north through the Msila region.

The hierarchical cluster analysis (HCA) is carried out with the same data used in the PCA (Fig. 3). The dendrogram obtained from the matrix of genetic distances of the ten regions of Algeria allows regrouping these populations in six classes. Geographical coherence is observed with the exception of class 5 in which there is a proximity of the region 9 with the region 6 (Constantine, Setif, and Guelma) which deserves to be exploited to better reveal this genetic proximity between these two regions. Our results obtained by HCA show that the gene frequencies of the ABO*O and K alleles and the RH^*R_2 haplotypes; and RH^*R_0 for the populations of Msila, the Great South, and the Region 9 have averaged much higher than the general average of these genetic frequencies compared to the rest of the Algerian regions. This genetic proximity between the population of Msila and the populations of the great south of Algeria as well as the population of the region 9 characterized by these biological markers (ABO*O, K, RH^*R_2, RH^*R_0) is confirmed by a hyper geometric test whose *P*-value is significantly lower than 5% (see Table 4) which is consistent with the geographical and historical aspect as well as the migratory flow of these populations.

Table 4
Test hyper geometric of Msila and the two regions (9 and10).

Genotype	Mean in category	Overall Mean	*P*-value
ABO*O	0.7459	0.6768	0.0386*
RH^*R_0	0.2828	0.2238	0.0315*
RH^*R_2	0.1499	0.0978	0.01414*

* $0.01 < P < 0.05$ significant.

4.2. Inter-population comparison

Based on the historical, geographical and cultural profile, 29 populations have been selected around the world for comparison between them and Msila, building a potential parent tri-hybrid model (North Africa, Middle East, and the shore of the Mediterranean). The gene frequencies of Msila population and other populations are presented in Table 5 used for comparison. Table 6 groups the genetic distances chosen in ascending order by

Table 5
Gene frequencies of Msila population and other populations.

Population	ABO*A	ABO*B	ABO*O	RH*R_1	RH*R_2	RH*R_0	RH*r	RH*r_1	K	References
Msila	0.1645	0.0934	0.7459	0.3725	0.12	0.2115	0.254	0.0201	0.0408	This work
Sardinia (Italy)	0.22	0.069	0.711	0.643	0.089	0.036	0.187	0.025	0.028	[a]
Greece 1	0.226	0.052	0.691	0.561	0.101	0.015	0.309	0.014	0.018	[b]
Greece 2	0.33	0.072	0.607	0.552	0.113	0.036	0.278	0.02	0.129	[c]
Spain 1	0.292	0.065	0.642	0.41	0.071	0.054	0.377	0.017	0.038	[d]
Spain 2	0.334	0.065	0.601	0.409	0.147	0.04	0.378	0.004	0.036	[e]
Balearic I.	0.249	0.045	0.706	0.476	0.012	0.032	0.363	0.003	0.046	[f]
France	0.262	0.06	0.677	0.426	0.13	0.02	0.402	0.009	0.042	[c]
Corsica 1	0.207	0.037	0.755	0.448	0.171	0.042	0.331	0.0000	0.028	[f]
Libya	0.225	0.132	0.643	0.412	0.133	0.11	0.329	0.008	0.055	[g]
Algeria	0.176	0.176	0.648	0.429	0.137	0.089	0.345	0.0000	0.049	[c]
Egypt 2	0.26	0.147	0.593	0.326	0.133	0.186	0.337	0.011	0.098	[g]
Egypt 1	0.222	0.104	0.674	0.463	0.14	0.234	0.157	0.005	0.045	[c]
Saudi Arabia 1	0.1618	0.1257	0.7138	0.3897	0.0996	0.2261	0.255	0.0000	0.061	[h]
Jordan	0.2881	0.1055	0.6064	0.408	0.1308	0.1137	0.2937	0.0538	0.0447	[i]
Palestine	0.3311	0.1325	0.5364	0.4817	0.1024	0.1439	0.269	0.0000	0.0197	[i]
Jordanian Nomads	0.2144	0.1231	0.6625	0.435	0.1043	0.0946	0.3137	0.0327	0.0268	[i]
Yemenite Southern Arabs	0.18	0.06	0.76	0.47	0.11	0.11	0.29	0.02	0.05	[j]
Yemenite Northern Jews	0.2	0.03	0.77	0.61	0.07	0.2	0.28	0.0000	0.015	[j]
Yemenite Southern Jews	0.14	0.08	0.77	0.48	0.16	0.07	0.24	0.02	0.005	[j]
Iraqi Northern Kurdish Jews	0.32	0.16	0.51	0.46	0.19	0.0000	0.28	0.02	0.033	[j]
Iraqi Southern Kurdish Jews	0.12	0.25	0.63	0.65	0.21	0.0000	0.07	0.0000	0.01	[j]
Iranian Kurdish Jews	0.25	0.22	0.53	0.52	0.22	0.0000	0.19	0.02	0.024	[j]
Syrian Kurdishs	0.27	0.17	0.56	0.45	0.11	0.07	0.36	0.0000	0.012	[j]
Iraqi Kurdishs	0.23	0.16	0.61	0.48	0.04	0.24	0.24	0.0000	0.033	[j]
Iranian Kurdishs	0.22	0.15	0.63	0.52	0.17	0.0000	0.21	0.0000	0.07	[j]
Turkey	0.286	0.149	0.565	0.482	0.171	0.05	0.21	0.014	0.01	[g]
Malta	0.257	0.052	0.691	0.505	0.151	0.039	0.308	0.0000	0.07	[g]
Corsica 2	0.204	0.041	0.755	0.488	0.098	0.075	0.323	0.009	0.036	[g]
Saudi Arabia 2	0.134	0.123	0.741	0.459	0.149	0.099	0.271	0.014	0.114	[k,l]

[a] Vona et al. [10].
[b] Tsiakalos et al. [11].
[c] Roychoudhury and Nei [12].
[d] Moreno and Moral [13].
[e] Miguel and PetitPierre [14].
[f] Vona et al. [15].
[g] Mourant et al. [16].
[h] Saha et al. [17]
[i] Taleb and Ruffié [18].
[j] Tills and Warlow [19].
[k] Abdelaal et al. [20].
[l] Chaabani et al. [21].

contribution to the population of Msila allowed us to share these 29 population in three categories of the closest to the population of Msila at the furthest distance, and that according frequencies obtained for the three polymorphic blood systems ABO, RH, and KELL: category I, whose genetic distance is less than 0.1 and which groups together 7 populations (Saudi Arabia1, Arabs of South Yemen, Egypt 1, Saudi Arabia 2, nomads of Jordan, Libya, Jews from South Yemen). Category II whose genetic distance is between 0.2 and 0.3 and which includes 12 populations (Corsica 2, Algeria, the Kurds of Iraq, Jordan, Egypt 2, Corsica 1, Malta, the Jews of North Yemen, Spain 1, France, Balearic I., Greece 1). Category III whose genetic distance is greater than 0.3 and which includes 10 populations (Kurds of Syria, Palestine, Kurds of Iran, Turkey, Spain 2, Sardinia (Italy), Greece 2, Kurdish Jews from the north of Iraq, the Kurdish Jews of Iran, the Kurdish Jews of southern Iraq) This tri-hybrid model was analyzed for seven potential parental populations, always based on the closest genetic distances to the Msila population, Middle Eastern populations (Saudi Arabia and South Yemen Arabs) who constitute the first parental strand potential and North African populations (Egypt and Libya) constitute the second strand. These four populations seem the most potential parents of the Msila population according to the parenting model built for this comparison, while for the third parental strand, which is the Mediterranean rim and particularly the northern shore of the Mediterranean (southern Europe), there is no potential parental link because the genetic distances between these populations and that of Msila seem to be far away, despite the presence of a historical and cultural link between the population of Msila and some populations of southern Europe.

The multidimensional analysis of our 30 populations brings us even closer to the vision of this trihybrid model (Fig. 4) and allows us to cut through these potential parental links that are still characterized by the study of these three polymorphic blood systems ABO, RH, and KELL. This PCA represents an overall variability of 64.47% projected on 3 axes. For Axis 1, we have the populations (Kurdish Jew of southern Iraq followed by the Kurdish Jews of Iran and in the end the Kurds of Iran) which are characterized by a good correlation for the B allele and the R_1 and R_2 haplotypes, opposing the populations (Spain 1, Balearic.I followed by the northern Yemeni Jews) which are characterized by a good correlation for the haplotype r and the O allele as well as partially the R_0 haplotype. For axis 2 we have the populations (M'sila, Saudi Arabia, Egypt 1, the Arabs of South Yemen and finally the Kurds of Iraq) which are characterized by a very good correlation coefficient very close to 1 (0.82) of the R_0 haplotype, this second axis put the latter populations in opposition to the group of populations (Greece 2, Spain 2, France, followed by Jordan, the Kurdish Jews of northern Iraq and the Kurdish Jews of Iran) which are characterized by a good correlation of the A allele and an acceptable correlation for the r_1 and R_2 haplotypes. This multidimensional analysis allows us to deduce that the

Table 6
Genetic distances between the population of Msila and some populations.

Population	Reynolds distance
Msila	0.0000
Saudi Arabia 1	0.0617
Yemenite Southern Arabs	0.1514
Egypt 1	0.1653
Saudi Arabia 2	0.1688
Jordanian Nomads	0.1791
Libya	0.1837
Yemenite Southern Jews	0.1898
Corsica 2	0.2043
Algeria	0.2092
Iraqi Kurdishs	0.2159
Jordan	0.2203
Egypt 2	0.2204
Corsica 1	0.2204
Malta	0.2564
Yemenite Northern Jews	0.2582
Spain 1	0.2676
France	0.2775
Balearic I.	0.2790
Greece 1	0.2943
Syrian Kurdishs	0.3002
Palestine	0.3017
Iranian Kurdish	0.3031
Turkey	0.3069
Spain 2	0.3125
Sardinia (Italy)	0.3384
Greece 2	0.3443
Iraqi Northern Kurdish Jews	0.3772
Iranian Kurdishs Jews	0.3883
Iraqi Southern Kurdish Jews	0.4527

population of Msila with the two parental groups potential North Africa (Libya, Egypt) and the Middle Eastern parent group (Saudi Arabia and the Arabs of South Yemen) constitute a single southern block characterized mainly by the high frequency of the O allele and the R_0 and R_2 haplotypes, as opposed to the northern block (Europe), characterized mainly by the high frequency of the A allele and the haplotypes r, R_1, and r_1 which has been demonstrated in most of the studies published in the past [22,23].

Table 7
Test hyper geometric of the population of Msila and the potential parents (Tri-hybrid Model).

Genotype	Mean in category	Overall Mean	*P*-value
ABO*O	0.6937	0.6578	0.0100*
RH*R_0	0.1744	0.0879	0.0001***
K	0.0619	0.0429	0.0333*
RH*R_2	0.1676	0.1261	0.0062**

* $0.01 < P < 0.05$ significant.

The hierarchical cluster analysis (HCA) is carried out with the same data used during the PCA (Fig. 5), the matrix of the genetic distances of the studied populations allow us to illustrate a dendrogram made of 3 classes:

- class 1 includes Kurdish Jews from southern Iraq, Kurds from Syria, Palestine, Kurdish Jews from Iran, Turkey, and Kurdish Jews from northern Iraq;
- class 2 includes Kurds of Iraq, Msila, Saudi Arabia 1, Egypt 1, Egypt 2, Saudi Arabia 2, Kurds of Iran, Libya, and Algeria;
- class 3 encompasses Balearic I., Corsica1, Malta, Corsica 2, the Arabs of South Yemen, Greece 1,the Jews of North Yemen, the Jews of South Yemen, Greece 1, Sardinia (Italy), nomads of Jordan, Jordan, Greece 2, Spain 2, Spain 1, and France.

According to the results obtained by our HCA, we notice that there is a geographical and cultural and even historical coherence in the majority of the classes obtained in particular the class 2 in which is the population of Msila which presents according to this HCA a great genetic similarity with that of the Middle East (Saudi Arabia) and that of North Africa (Egypt). This genetic similarity marked by the high genetic frequencies of the O allele and the K allele and especially the R_0 haplotype, these genetic markers have averaged well above the general average of these same biomarkers for the rest of the compared populations. This genetic proximity between the populations of Msila, Saudi Arabia, and Egypt characterized by these genetic markers ABO*O, RH*R_0, K is confirmed by a hyper geometric test presented in Table 7, whose *P*-value is

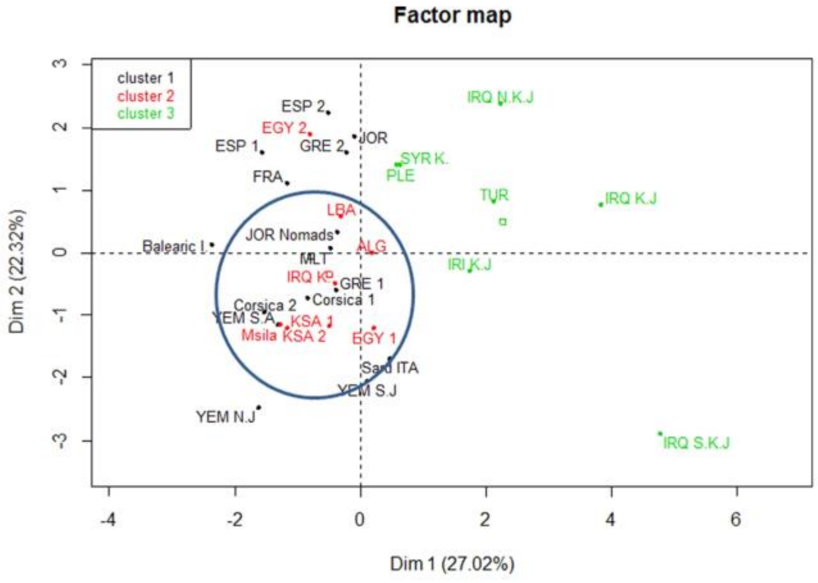

Fig. 4. Principal components analysis for Msila population's and 29 populations tested for ABO, RH and KEL.

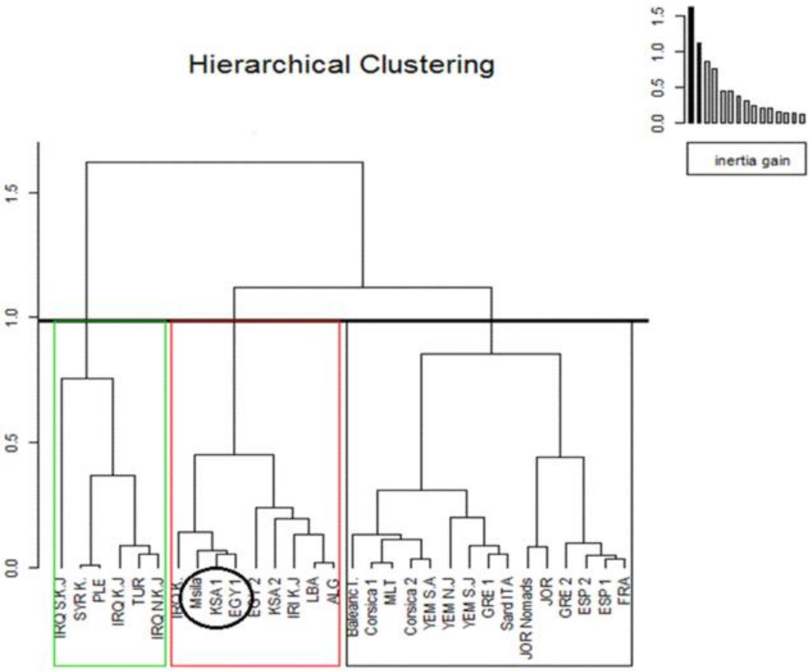

Fig. 5. The hierarchical cluster analysis for Msila population's and 29 populations tested for ABO, RH and KEL.

significantly lower than 5% which is strongly correlated with the potential parental hybrid model based on the historical, geographical and cultural profile of these populations, on the other hand, concerning the northern shore of the Mediterranean (southern Europe) which is characterized, according to our results obtained from the HCA, by high frequencies of the A allele and the haplotypes R_1, r, do not seem to correlate with our parental model potential, therefore the north shore of the Mediterranean (southern Europe) does not represent a potential parental link with the Msila population.

5. Conclusion

The results concerning the exploration of these three ABO,RH, and Kell erythrocyte blood group systems to characterize the population of Msila demonstrates that the genetic profile of this population at the Algerian scale on one side is close to the populations of the great south of Algeria going south-east, by sharing the map of Algeria in two blocks: a southern block characterized by a high frequency of the O allele and R_2 haplotypes and partially R_0 compared to the northern block which is constituted by the eight mapping regions developed by Lefevre-Witier et al. [3]. This northern block which is characterized by a high frequency of the A allele and haplotypes R_1 and partially r. This genetic profile characterized by the high frequencies of the A allele and the R_1 and R haplotypes compared to the southern block of Algeria, put the Algerian north in a genetic position close to southern Europe (north shore of the Mediterranean). This synthesis is consistent with the historical experience and migration flow and cultural profile between the population of Msila and the rest of Algeria. On the other hand, at the international scale, a potential trihybrid parental model has been developed in which the Msila population demonstrates genetic similarity with the Middle East (Saudi Arabia and South Yemen Arabs) as a potential first parent followed by northern Africa (Egypt and Libya) as a potential second parent, while the north shore of the Mediterranean (southern Europe) does not present itself as a potential third parent to the Msila population according to our potential trihybrid parental model based on a historical, geographical and cultural profile.

Finally, if we allow ourselves to draw a retrograde route of the population of Msila over time, according to the results obtained from the genetic study of the three-erythrocyte polymorphic systems ABO, RH, and KELL, based on its history and its geography as well as its cultural heritage it is stipulated that its current genetic profile starts from the center of Algeria down to the great south of Algeria going south-east to Libya and then back to Egypt. As far as Saudi Arabia one goes down to the south ending in the south of Yemen.

Disclosure of interest

The authors declare that they have no competing interest.

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