Association of ABO, Rh Blood Groups Systems with Lipids and other Anthropometric Co Variables as Predictors of Cardiovascular Risk in NWFP, Pakistan

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Aims and Objects: The present study was carried out to find the possibility of association of lipid profile with ABO Rh blood groups and other anthropometric co- variables as cardiovascular risk. **Material and Methods**: A community-based investigation was carried out on lipid profiles and blood groups of selected population of rural and urban areas of Peshawar, NWFP on total of 1304 subjects out of which 548 were females and 756 were males. Age ranged from 16-75 years. Due emphasis was laid in the study on anthropometric parameters (age, height, body weight and body mass index) blood pressure and dietary parameters. **Results:** Blood grouping revealed distribution of various blood groups in the order of their predominance being B>O>A>AB. The Rh- positive subjects were 94.6% of the total. Sex wise analysis of anthropometric data, blood pressure including pulse rate and lipid profiles prior to partitioning by Rh factor revealed only sporadic significant differences among the various ABO blood phenotypes. When the ABO phenotypes were partitioned according to Rh factor and gender, substantially more significant Rh factor associated differences were seen among the ABO phenotypes. **Conclusion:** Most of the lipid profile parameters for the sample do not provide enough evidence of hyperlipidemia and cardiovascular risk. The A and A B Phenotypes show lesser long term risk if any. The B and O phenotypes have relatively higher tendency of adverse lipid/lipoprotein metabolism and hence invite greater attention from therapeutic point of view. There is no evidence of predisposition of phenotype A as a co marker of risk of cardiovascular disorders.

Key words: Blood groups, risk markers, hyperlipidemia, cardiovascular risk

The major killer of people above the age of 36 years is coronary heart disease (CHD) which is usually considered as a disease of ageing, arteriosclerosis, hypertension and different forms of cardiovascular diseases (CVD). They are related to various risk factors particularly high levels of serum lipids, lipoproteins, diabetes mellitus, dietary habits, lack of exercise and obesity[1] as well as emotional stress[2]. Many efforts have been made in the past to assess the extent to which the ABO blood groups and their subgroups reflect risk of CVD along with analysis of lipid profile and environmental risk markers of cardiovascular impairment[3,4,5]. During the last several decades there has been ample focus on identification of phenotypic and genotypic markers as predictors of hyperlipidemic condition and hence that of impending threat of CHD and related disorders, particularly involving possible correlation between hyperlipidemia and ABO blood groups[6,7,8,9,10,11,12,13]. Investigations have not been confined to association with the ABO system but has also been extended to include Rh system and subgroups of ABO system[14,15]. The present study was designed to focus on community-based analysis of lipids/lipoproteins, anthropometric parameters, blood pressure parameters and their association with the ABO and Rh blood groups as indicators of risk of CVD in a selected population sample from Peshawar, NWFP, Pakistan.

Material and Methods

A total of 1304 subjects, 548 females and 756 males, were screened carefully and only healthy individuals were included in the study. The subjects included belonged to both rural and urban areas of Peshawar including tribal territory of NWFP. The age ranged from 16-75 years. A detailed history Proforma was duly completed in all subjects enquiring especially regarding their occupation status, personal health history, dietary habits and physical activity.

Body weight (kg), height (cm), systolic and diastolic (SBP, DBP) blood pressure (mmHg) and pulse (beats/min) of the selected healthy subjects were recorded. All subjects were fasted for 12-14 hrs prior to collection of blood for blood groups and lipid profiles/lipoproteins analysis. All the analytical work was carried out in PMRC research center, KMC, Peshawar from 2001 to 2002.

Determination of blood groups:

Blood grouping was done by the antigen-antibody agglutination test. The antisera used were obtained from Plasmatec (Kent, UK). For determination of Rh factor, Plasmatec anti-D (1gm) Lo-Du and LoDu2 monoclonal reagents were used.

Biochemical analysis:

Total serum cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C) and triglycerides (TG) were determined by enzymatic colorimetric method using Elitech Kit (Brussels). The optical density of the sample and standard was read against a blank on a spectrophotometer (Irma colorimeter, Japan) in each case at different wavelengths specified by the kit used. Differences among the various

blood groups and sexes within blood groups were determined by student's t-test.

Results

Blood Groups distribution: Table 1 shows distribution of ABO blood groups by number and percentage in the total population and according to gender. The order of distribution of the blood groups in the total sample was B>O>A>AB. B group being dominant in the males and O in the females. The group AB was represented in approximately a third of the subjects only.

Anthropometric measurements: No significant differences in height existed among the various blood groups. However, sex-specific differences ($P<0.05$) were noted within all blood phenotypes (Table-II, foot note), the males being taller than the females. Regarding body weight, only the AB and B groups differed, the AB males being significantly heavier than the B males ($P<0.05$) (Table 2). Within all individual blood groups, the males were significantly heavier than the females (Table 2) footnote.

Blood Pressure: No significant differences in Systolic blood pressure, diastolic blood pressure and pulse rate was observed in the blood groups (Table II). However, statistically significant differences existed between the sexes within each of the B and O groups for SP ($P<0.05$,Table 2,footnote) and A and O groups for DP ($P<0.05$,Table 2,footnote).The males in these three groups had higher SP and DP than the females. The differences in pulse rate remained insignificant both among the blood groups and between sexes within blood groups (Table 2).

Lipids and Lipoproteins: No statistically significant differences were noticeable in TC either among the various blood groups or between sexes within individual blood groups (Table 2). Mean HDL-C levels were not significantly different among the various blood groups (Table 2). However, between sex differences existed only within the B and O groups, the females in the both groups showing higher HDL-C than the male subjects ($P< 0.05$ Table 2,footnote). LDL-C levels were significantly higher in the O subjects compared to both the A and B groups. Not only did the O males have higher LDL-C level than the A and B males, the O females too had higher level than the A females. Between sex differences within the individual blood groups were not evident (Table 2). TG showed significant differences only between the A and O groups. Here, only the females differed; the A females showing higher TG level than the O females ($P<0.05$, Table 2). Between sex differences were significant only within the O groups; the males having higher levels than the females (Table 2,footnote).

Differences Among the ABO Groups Based on Rh factor: When the data was analyzed by partitioning the ABO phenotypes according to Rh factor, far greater significant differences were discernible reflecting an association of the various parameters with the Rh factor. (Table 2).

Anthropometric Parameters:

Height: Statistically significant differences were observed in height of group A subjects on comparison with B, AB and O phenotypes. The Rh-ve A females turned out to be significantly taller than the corresponding AB and B females. The Rh+ve A males were significantly shorter than AB males. Within any given blood group, no Rh-ve dependent same sex differences were evident.

Body weight: The type A subjects also showed significant Rh factor associated differences in bodyweight in comparison with all other phenotypes. Most of the subjects showing the differences were Rh+ of either gender. The weight of Rh+ A males was less than that of Rh+ AB and O males.($P<0.001$). Within individual blood groups, neither the males nor the females showed Rh-dependent differences (same sex). Sex dependent differences within any blood group were noted only for the Rh+ A and O males and females, the males being heavier.

Blood pressure: Significant differences in systolic blood pressure were evident between the Rh-veA and O phenotypes only. Here Rh-veA males had lower SP than Rh-ve O males. Between sex differences (within Rh group) were significant only for Rh-ve males and females within both A and O groups, the Rh-ve males showing higher SP than Rh-ve females.

Significant differences in Diastolic Blood pressure of type A subjects were discernible relative to the AB and B phenotypes only. The association was with the Rh-ve factor. The Rh-veA males had higher DP than the corresponding A females ($P<0.05$). Only the AB Rh+ males had significantly higher diastolic blood pressure the Rh+veA males.

Pulse Rate: The pulse rate for most subjects of all blood groups was close to the average value for healthy adults (72/min). Notable exceptions were that the AB Rh-ve males (84/min) and B Rh-ve males (86/min). Significant differences were evident for the A subjects versus AB, B, and O groups. The A +ve males had significantly lower pulse rate than the corresponding males of the AB group. The A-ve males had lower pulse rate than the O-ve males. The AB-ve males had significantly higher pulse rate than the O-ve males ($P<0.05$).

ABO SYSTEM, LIPIDS AND LIPOPROTEINS

Total cholesterol (TC): :The values of **TC** for both sexes were within the acceptable reference range (Elitech Reference Values). With the exception of A: O and B: O groups, none of the other groups showed significant Rh associated differences. The Rh+ A females had lower TC than the corresponding O females with a similar difference between the Rh+ B and O males ($P< 0.05$).

High Density lipoprotein cholesterol (HDL-C): The mean levels of HDL-C for most of the subjects of the various blood types were in the standard risk reference range (35-55 mg/dl for males, 45-65 mg/dl for females, see Methods). Significant Rh associated differences were recoded for A and AB groups compared to the other

groups. Most differences were associated with Rh- males had higher HDL-C than the AB, B and O Rh-ve males. Similarly, the A Rh-ve females had significantly higher mean HDL-C compared to the O Rh-ve females. The mean levels for A Rh+ males were significantly lower than that of the AB Rh+ males. The groups AB and O also differed, where the AB Rh+ males had higher mean HDL-C than the O Rh+ males.

Rh-specific differences (same sexes) existed within group A and AB only. The Rh- males had higher HDL- C than the RH+ males. The situation was reversed for the AB group; the AB RH+ males had higher HDL-C than the RH- males. Between sexes differences in HDL-C level were noted within A, B and O groups only.

Low-Density lipoproteins Cholesterol (LDL-C)

The LDL-C levels for most of the subjects were in the acceptable reference range. However the type A+ males and females had significantly lower levels than O+ve males and females. Similarly the B+ve males had lower LDL-C levels than O+ve males, Rh+ve males had higher LDL-C levels than Rh-ve males.

Triglycerides:(TG): The TG levels of the males of all the blood types were generally at the higher end of the reference range. The levels for the female subjects of all blood phenotypes were either slightly above or near the upper end of the reference range. No statically. Significant differences were recorded either among the blood groups or the same sexes within given blood groups between sexes differences within blood groups were evident between the **O Rh+** males and females only.

Body-Mass Index (BMI): The BMI of all blood types of both genders were in the normal range. The BMI of only the AB females marginally exceeded the normal BMI range, which was also significantly different from the BMI of O females.

Table 1 Distribution of various blood groups by sex in the total sample of subjects

Blood Groups	%	Male	Female	Total	Within group %	
					Male	Female
A	28.5	218	154	372	58.60	41.13
B	30.1	246	154	400	61.50	38.50
AB	10.1	078	066	144	54.17	45.80
O	29.7	214	174	388	55.15	44.80
Total	100	756	548	1304		

Discussion

The ABO and Rh blood system has been associated by majority of workers with a variety of diseases including immunological disorders and hence is considered to be a marker of impending health hazards. The most prevalent view is that the A phenotype has far greater susceptibility for myocardial infarction, atherosclerotic peripheral vascular disease and several other types of CVD than the non A phenotypes, particularly the O phenotypes[16,17,18,20]. This observation has received substantiation from statistically backed evidence for an association between ABO system and TC, LDL-C, HDL-C and TG as well as data on various Anthropometric and blood pressure measurements that are known to be major CVD risk factors[6,11,12,14,18,19,20,21].

In the present study also, no significant differences could be discerned in mean levels of TC, LDL-C, HDL-C and TG among the various blood phenotypes. Whereas the ABO system did not show an independent association with lipids, lipoproteins and other variables tested in the present work, the ABO heterogeneity in the examined parameters became evident only when specific and sex-specific.

Several country reports show that HDL-C bears an inverse association with CHD[22,23,24,25]. Castelli and Leaf[26] have also shown in the Framingham Heart Study (Massachusetts, USA) that increased levels of HDL-C are associated with decreased risk of CHD in both men and women. The prevalence of standard risk levels (border line) of HDL-C in Peshawarites, therefore, is worthy of attention from the standpoint of a population trend that may foreshadow cardiovascular risk. This trend in combination with elevated levels of TG (as have been observed in the present study) can have serious health consequences.

The present investigation was designed to primarily examine lipid/lipoprotein profile of a local population sample along with their possible correlation with the ABO and Rh blood groups as co markers of risk of CVD-risk. With some exceptions, the population means of the lipids and lipoproteins, Anthropometric and blood pressure parameters do not exceed the acceptable limits. notable exceptions in this regard are the observed levels of TG and HDL-C that may be of some concern. Furthermore significant Rh factor-dependent sex-specific differences among the various blood groups and within individual blood groups exist in respect to the parameters examined. Yet, there is hardly any reason to support the view that the A blood phenotype is a predictor of hyperlipidem and hence of cardiovascular risks. In fact, the results of this study suggest greater predilection of the B and O groups, in the long term, for an adverse lipid profile. Thus, it is these groups rather than the A phenotypes that invite greater vigilance from a therapeutic standpoint.

Conclusion

1. Most of the lipids and lipoproteins parameters for the Peshawar sample do not provide enough evidence of hyperlipidemia.
2. The A and AB phenotypes show lesser long-term risk.
3. The B and O phenotypes have relatively grater tendency of adverse lipid/lipoprotein metabolism and hence invite greater attention from the therapeutic point of view.

There is no evidence of predisposition of the A phenotype as a co-marker of risk of cardiovascular disorders.

Table 2. Mean± SEM of various anthropometric parameters of ABO phemotypes according to sex and prior to partitioning by Rh factor (SIGNIFICANT DIFFERENCES ARE DENOTED IN **BOLD, P<0.05)**

Parameter	A		B		AB		O	
	Male	Female	Male	Female	Male	Female	Male	Female
Number	99	63	118	62	36	28	92	78
Height [a]	167.9	154.4	168.7	155.4	170.8	150.3	169.9	154.3
(cm)	1.1	1.5	1.3	1.5	1.5	3.6	1.3	1.5
Weight [b]	68.3	61.0	**67.2**	63.1	**72.9**	63,2	**68.8**	61.7
(Kg)	1.2	1.3	0.9	1.7	2.3	2.8	1.2	1.3
SBP [c]	119.1	116.8	120.9	115.6	120.2	118.5	121.4	115.5
(mmHg)	1.3	1.5	1.3	2.0	1.7	2.8	1.4	1.3
DBP [d]	78.6	76.0	79.0	76.3	80.1	77.0	78.5	75.3
(mmHg)	0.9	0.9	0.9	1.1	1.2	1.6	0.9	0.9
Pulse	76.6	0.9	76.4	76.0	78.8	76.2	76.2	75.6
(Per min.)	0.8	1.2	0.8	1.1	1.3	1.2	0.7	0.8
TC	176.1	172.1	171.0	175.0	175.9	177.0	177.1	179.4
(mg/dl)	3.6	3.3	2.8	4.0	5.1	6.4	3.0	4.2
HDL-C [e]	47.2	49.5	47.4	50.5	50.0	48.7	46.6	49.6
(mg/dl)	0.9	0.9	0.7	1.3	1.6	1.7	1.0	1.1
LDL-C	**93.7**	**93.1**	**93.7**	95.4	95.7	99.3	**101.4**	**104.2**
(mg/dl)	2.9	3.3	2.5	3.7	5.1	5.8	2.8	4.1
TG [f]	159.1	**147.9**	146.6	138.6	145.6	146.1	150.4	**127.7**
(mg/dl)	7.4	7.7	5.2	8.4	9.6	9.1	5.9	4.9

A between sex differences (P<0.05)in height, b=between sex differences(P< body weight within all ABO, c=between sex differences(P<0.05)in SBP within B&O groups, d between sex differences(P<0.05) in DBP within A&O groups, e=between sex differences(P<0.05) in HDL-C within B & O groups, f=between sex differences(P<0.05)in TG within O group.

References:

1. Goldberg R.J. Coronary heart disease: epidemiology and risk factors. In: Prevention of coronary heart disease. Eds. Ockene, I.S and. Ockene, J.K, IST ed; Little, Brown and Co; London, 1992;P40
2. Kabat-Zinn J. Psychosocial factors: their importance and management. In: Prevention of coronary heart disease. Eds. Ockene, I.S. and Ockene, J.K; Ist. ed. Little, Brown and Co, London.1992; P- 299-334.
3. Akhund I A, Akhund A A, Alvi I.A, Hafeezullah, Ansari A K. 1998. ABO blood group and serum lipids in patients with ischaemic heart disease. JAMC, 1998; 10:14-16.
4. Akhund I A, Soomro M B.. ABO blood groups and peripheral vascular disease. Med. Channel Issue, 1999; 2, No. 5, April-June.
5. Soomro, M.S, Karira K.A. Prevalence of ABO blood groups in myocardial infarction with relation to lipid lipoproteins. Pakistan J Med Sci. 2000; 16(2): 78-80.
6. Langman, M.J.S, Elwood PC, Foote J, Ryrie D.R. ABO and Lewis blood groups and serum cholesterol. Lancet.1969; 2:607-609.
7. Mayo O, Wiesenfeld S L, Stamatoyannopoulos G, Fraser G.R. Genetic influences on serum cholesterol level. Lancet.1971; 2:5545.
8. Hagerup L,. Hensen PF, Skov F. Serum cholesterol, serum triglyceride and ABO blood groups in a population of 50-yearold Danish men and women. Am. J.Epidemiol.1972; 95:99-103.
9. Allan T.M. ABO blood groups and arteriosclerosis. Arteriosclerosis 1973; 18:347-351.
10. Polychronopoulou A, Miras CJ, Trichopoulous D. Lipoprotein types, serum cholesterol and ABO blood groups. Br .J .Prev. Soc. Med. 1974; 28:60-62.
11. Fox MH, Weber LS, Thurmon TF, Berenson G.S. ABO blood group association with cardiovascular risk factor variables II. Blood pressure, obesity and their Anthropometric covariable. The Bogalusa Heart Study. Hum.Biol.1986; 58:549-584.
12. Gillum R.F. 1991. Blood pressure and obesity in adolescents. J Natl. Med.Assoc.1991;83 (8): 682-688.
13. Contiero E, Chinello G E. Serum lipids and lipoprotein associations with ABO blood groups. Anthropol. Anz.1994; 52(3): 221-230.
14. Wakely E.J. Blood group A sub-groups and serum cholesterol. Cardiovasc.Res.1973; 7: 679-683.
15. Hein HO, Sorensen H, Suadecani P, Gyntelberg, F. The Lewis blood group-a new genetic marker of ischaemic heart disease. J Int Med 1992; 232: 481-487.
16. Meeran K, Bloom SR. Lewis phenotypes insulin resistance and risk of ischaemic heart disease. Br. Heart J.1994; 71: 305-306.
17. Ismagilov M.F, Petrova S.E. ABO blood group system and vegetative-vascular disorders in children (in Russian, English summary). Zh. Nevropatol. Psikhiatr.1981; 81:1487-1488.
18. Meshalkin E.N, Okuneva, Iu.A, Vel' tmander, N.N.ABO and Rh blood groups in cardiovascular pathology (in Russian, English summary). Kardiologiia.1981; 21(4): 46-50.
19. Wong F L, Kodama K Sasaki H. Longitudinal study of the association between ABO phenotypes and total serum cholesterol level in Japanese cohort. Genet. Epidemiol. 1992; 9(6): 405-418.
20. Green D, Jarret O, Ruth K.J, Folsom A, Liu K. Relationship among Lewis phenotype, clotting factors and other cardiovascular risk factors in young adults. J. Lab. Clin. Med.1995; 125(3): 334-339.
21. Fox M.H., Weber L.S., Srinivasan S.R. O blood group association with cardiovascular factor variables I. Serum lipids and lipoproteins-The Bogalusa Heart study. Hum. Biol.1981; 53:411.
22. Borecki I.B, Elston R C, Rosenblum P.A. ABO association with blood pressure, serum lipids and lipoproteins and Anthropometric measures. Hum. Hered.1985; 35(3): 161-170.
23. Miller N.E, Ford O.H, Thelle D.S, Mojo O.D. The Tromso Heart Study: High-density lipoprotein and coronary heart disease: a prospective case-control study. Lanct.1977; 1:965-970.
24. WHO Expert Committee on the prevention of Coronary Heart disease. Prevention of coronary heart disease. World Health Organization Technical Report.1982; Series No.678 Geneva: World Health Organization.
25. Goldbourt U, Holtzman E, Neufeld H.N. Total and high-density lipoprotein cholesterol in the serum and risk of mortality: evidence of a threshold effect. Br. Med. J.1985; 290:1239-1243.
26. Cstelli W, Leaf A. Identification and assessment of cardiac risk - an overview. Card. Clin.1985; 3:171-178.