

Original Research Article

Prevalence of ABO-Rh positive blood groups in relation to hypertension and type 2 diabetes mellitus among the male urban population of Deoghar, Jharkhand: a cross sectional study

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ABSTRACT

Background: Hypertension is the subsequent elevation of the systemic arterial pressure to a level that places the patients at increased risk for target organ damage. Type 2 diabetes mellitus is characterised by the common phenotype of hyperglycemia due to genetic and metabolic defects in insulin action and/or secretion.

Methods: This study was performed to evaluate the prevalence of ABO-Rh positive blood groups among the male hypertensive and type 2 diabetic urban population of Deoghar. It was a cross-sectional population based study. 356 hypertensive and 425 type 2 diabetic male subjects were selected based on inclusion and exclusion criteria. Their basal blood pressures were determined using palpatory and auscultatory method. The random blood glucose levels of the subjects were estimated and their blood groups were also determined using slide haemagglutination technique.

Results: Among the hypertensive subjects 'O' Rh positive was the most prevalent (41%), followed by 'B' Rh positive (34%), 'A' Rh positive (17%) and lastly 'AB' Rh positive blood group (8%). Again, among the type 2 diabetic subjects 'B' Rh positive was most prevalent (45%), followed by 'O' Rh positive (36%), 'A' Rh positive (12%) and finally 'AB' Rh positive blood group (7%).

Conclusions: This study concludes that 'B' Rh positive and 'O' Rh positive blood groups are more prevalent as compared to other ABO-Rh positive blood groups among the male hypertensive and type 2 diabetic urban population of Deoghar. Thus, the persons belonging to these two blood groups should take adequate precautions since their childhood against these co-morbidities as they are more prone to develop them.

Keywords: Hypertension, Type 2 diabetes mellitus, ABO-Rh, Blood group

INTRODUCTION

Hypertension and diabetes mellitus are the two most important co-morbidities affecting people worldwide. Hypertension is the subsequent elevation of the systemic arterial pressure to a level that places the patients at increased risk for target organ damage. Diabetes mellitus is a clinical syndrome characterized by hyperglycaemia due to absolute or relative deficiency of insulin. Several distinct types of diabetes mellitus are caused by a complex interaction of genetics and environmental factors. A blood group system consists of a group of

antigens encoded by alleles at a single gene locus or at gene loci so closely linked that crossing over does not occur or is very rare.

An individual having a blood pressure of more than or equal to 130/80 mmHg should be considered hypertensive and he or she should be adequately treated. In children and adolescents, hypertension generally is defined as systolic and/or diastolic blood pressure consistently 95th percentile for age, sex and height. In 2017 American health association has updated blood pressure classification and it recommends blood pressure

criteria for defining elevated state which is a common occurrence even among the young individuals and is one of the leading causes of the global burden of the disease (Table 1).

Table 1: Classification of blood pressure (source: American heart association guidelines, 2017).

Blood pressure category	Systolic blood pressure (mmHg)	Diastolic blood pressure (mmHg)
Normal	<120	and <80
Elevated	120-129	and < 80
Hypertension stage 1	130-139	or 80-89
Hypertension stage 2	≥140	or ≥90

Hypertension is a significant public health concern and is one of the major causes of premature deaths worldwide. An estimated 1.13 billion people worldwide with 1 in 4 women and 1 in 5 men suffers from hypertension. Fewer than 1 in 5 people have well-controlled hypertension and more than 9 million deaths are associated with hypertension.¹ Studies suggest that hypertension increases the risk of cardiovascular disease by 10 fold and cigarette smoking increases the risk by at least threefold. Hypertension is a silent killer which leads to myocardial infarction, coronary artery disease, congestive heart failure, ischemic and hemorrhagic stroke, renal failure, peripheral arterial disease etc. Hypertension may cause end-organ damage in both women and men, and the risk increases in proportion to the magnitude of blood pressure in both sexes. Although the risk of death from coronary artery disease is at least three times as great for men as for women before menopause, the relative risk for women increases significantly after menopause. Studies have indicated that estrogen deficiency significantly increases the risk of cardiovascular disease in woman.

On the other hand, diabetes mellitus is the most common metabolic disorder affecting people worldwide both in developing and developed countries. Distinct genetic and metabolic defects in insulin action and/or secretion give rise to the common phenotype of hyperglycemia in type 2 diabetes mellitus. Several pathological processes are involved in the development of diabetes that range from autoimmune destruction of the β cells of the pancreas with consequent insulin deficiency to abnormalities that result in resistance to insulin action.² The worldwide prevalence of diabetes mellitus has risen dramatically over the past two decades, from an estimated 30 million cases in 1985 to about 422 million cases in 2021, the majority living in low-and middle-income countries, Both the number of cases and the prevalence of diabetes have been steadily increasing over the past few decades.³ Based on current trends, the International Diabetes Federation projects that 592 million individuals will have diabetes by the year 2035 and which is

expected to increase to 693 million in 2045.⁴ Moreover, about 183 million people worldwide are unaware that they have diabetes. Asia is a major area of the rapidly emerging type 2 diabetes mellitus global epidemic, with China and India being the top two epicentres. The number of people with diabetes mellitus in India currently around 40.9 million is expected to rise to 69.9 million by 2025.⁵

In 1901 the 'ABO' blood group system was discovered by Karl Landsteiner. ABO and Rh blood group antigens are the major human blood group system antigens. The blood type of an individual defined by small carbohydrate epitopes depends on the presence or absence of genes A and B. The gene is positioned on chromosome 9q34 and consists of 7 exons spread over 18 kb called ABO blood groups.⁶ The ABO system contains four major ABO phenotypes 'A', 'B', 'O' and 'AB' which are determined by presence or absence of antigen A (α) and/or antigen B (β) on the red blood cells. The Rh system is the second most important blood group system in transfusion medicine because antigen-positive red blood cells frequently immunise antigen-negative individuals through transfusion and pregnancy. Inheritance of Rh antigens is determined by a complex of two closely linked genes: one encodes the protein carrying D antigen (RhD); the other encodes the protein carrying C or c and E or e antigens (RhCE). Red blood cells (RBC) from Rh positive people have both RhD and RhCE, whereas Rh negative RBCs have only RhCE. ABO and Rh gene phenotypes vary widely across races and geographical boundaries and the resultant polymorphism remains important in population genetic studies, estimating the availability of compatible blood, evaluating the probability of hemolytic disease in the new born, resolving disputes in paternity or maternity and even for forensic purposes.⁷ The frequency of ABO and Rh phenotypes in different populations has been extensively studied and different studies have claimed to have found some association of blood groups with diseases such as duodenal ulcer, gastric cancer, urinary tract infection, salivary gland tumour, coronary heart disease, Rh incompatibility, ABO incompatibility of newborn along with others.^{8,9}

Aim and objectives

Objective of current study were to evaluate the prevalence of ABO-Rh positive blood groups among the male population suffering from hypertension and type 2 diabetes mellitus in urban Deoghar, Jharkhand. This study was formulated with an aim to know whether a particular blood group was more prevalent or common among the hypertensive and type 2 diabetic population as compared to others as blood group antigens are hereditary determined and play a vital role in disease susceptibility along with transfusion safety, understanding population genetic studies, researching population migration patterns, inheritance pattern, medico legal issues, disputed paternity and others.

METHODS

This study was a cross sectional population based study which was carried in during the period from 20 February, 2020 to 30 September, 2020 for duration of around seven and a half months in the department of physiology of all India institute of medical sciences Deoghar. This study was performed in accordance with the required ethical principles and guidelines. The written and informed consent of the subjects was obtained prior to collection of data.

The inclusion criteria for the study were as follows. For inclusion in the study all ABO-Rh positive blood group male subjects of 30 to 60 years were selected. Secondly, for determining the prevalence of ABO-Rh blood group among hypertensives only those subjects were selected who had hypertension and were on anti-hypertensive treatment for at least the last two years and finally, for determining the prevalence of ABO-Rh blood group among the subjects suffering from type 2 diabetes mellitus only those subjects were selected who had type 2 diabetes and were on hypoglycaemic treatment for at least the last two years. On the other hand the exclusion criteria of the study were as follows. Firstly, all the ABO-Rh negative blood group subjects were excluded from the study. Secondly, all female individuals of any blood group as well as both the male and female subjects suffering from both hypertension and type 2 diabetes mellitus at the same time as well as suffering from any other cardiovascular, endocrinal, neurological or haematological disease or co-morbidities other than hypertension or type 2 diabetes mellitus were excluded from the study.

A total of 781 male subjects who were residents of Daburgram, Towerchowk and their neighbouring urban areas in Deoghar, Jharkhand were selected based on inclusion and exclusion criteria by purposive sampling. Out of these 781 subjects, 356 subjects were suffering from hypertension and the rest 425 subjects were suffering from type 2 diabetes mellitus. The blood pressure and the 'ABO-Rh' blood group of the hypertensive subjects as well as the random blood glucose level and 'ABO-Rh' blood group of the type 2 diabetic subjects were determined in the following ways.

Determination of blood pressure

The basal blood pressures of the subjects were determined using palpatory method and auscultatory method for blood pressure measurement by using manual mercury sphygmomanometer in sitting posture.

Estimation of random blood glucose level

Under all aseptic and antiseptic measures, random blood glucose was estimated (Table 2) using glucometer (OneTouch select simple blood glucose monitoring

system, LifeScan Europe, division of Cilag GmbH International, 6300 Zug, Switzerland).

Table 2: Criteria for the diagnosis of diabetes mellitus (source: American diabetes association, 2011).

Criteria
Symptoms of diabetes plus random blood glucose concentration ≥ 11.1 mmol/l (200 mg/dl) or
Fasting plasma glucose ≥ 7.0 mmol/l (126 mg/dl) or
Glycosylated haemoglobin (HbA1C) $> 6.5\%$ or
Two-hour plasma glucose ≥ 11.1 mmol/l (200 mg/dl) during an oral glucose tolerance test.

Determination of blood groups

Blood group was determined using slide haemagglutination technique. In this technique, anti-A and anti-B serum were used for ABO blood group determination by detecting A and B antigens. Interpretation of result by slide haemagglutination technique (refer table 3). In the same way Rh grouping of the blood was done by using anti-Rh (or anti-D) serum.

Table 3: Interpretation of results by slide haemagglutination technique.

Reagents		Interpretation
Anti-A	Anti-B	Blood group
+	-	'A'
-	+	'B'
+	+	'AB'
-	-	'O'

Key: '+' = agglutination, '-' = No agglutination.

For all the statistical purposes Microsoft office excel 2007 was used in the study.

RESULTS

In current study the following results were found. For determination of prevalence of ABO-Rh blood groups among subjects suffering from hypertension: 148 subjects out of 356 hypertensive subjects belonged to 'O' Rh positive blood group, so the prevalence of blood group 'O' Rh positive among the hypertensive subjects is found to be 41%. 120 subjects out of 356 hypertensive patients belonged to 'B' Rh positive blood group, so its prevalence is 34%. 60 hypertensive subjects out of 356 hypertensive subjects belonged to 'A' Rh positive blood group, so its prevalence is 17%. 28 subjects out of 356 hypertensive subjects belonged to 'AB' Rh positive blood group, so its prevalence is 8% (Figure 1, Table 4).

For determination of prevalence of ABO-Rh blood groups among subjects suffering from type 2 diabetes

mellitus: 192 subjects out of 425 type 2 diabetic subjects belonged to 'B' Rh positive blood group, so the prevalence of blood group 'B' Rh positive among the type 2 diabetic subjects is found to be 45%.

Table 4: This table shows the prevalence percentage of ABO-Rh positive blood group in male hypertensive subjects (n=356).

Blood group (ABO-Rh positive)	N	%
'O'	148	41
'B'	120	34
'A'	60	17
'AB'	28	8

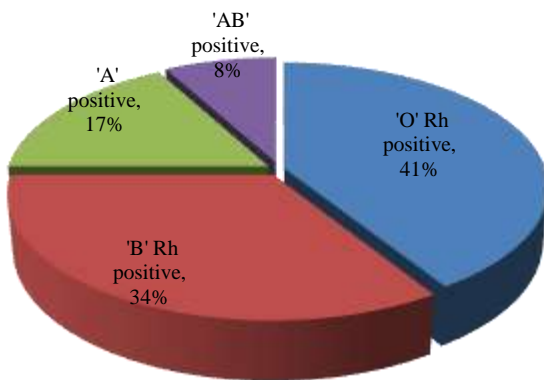


Figure 1: This figure shows the prevalence percentage of ABO-Rh positive blood groups among the male hypertensive subjects.

154 subjects out of 425 type 2 diabetic subjects belonged to 'O' Rh positive blood group, so its prevalence is 36%. 51 type 2 diabetic subjects out of 425 type 2 diabetic subjects belonged to 'A' Rh positive blood group, so its prevalence is 12%. 28 subjects out of 425 type 2 diabetic subjects belonged to 'AB' Rh positive blood group, so its prevalence is 7% (Figure 2, Table 5). It was seen that the blood groups 'B' Rh positive and 'O' Rh positive are more prevalent among the subjects suffering from hypertension or type 2 diabetes mellitus as compared to 'A' Rh positive and 'AB' Rh positive blood groups (Figure 3).

Table 5: This table shows the prevalence percentage of ABO-Rh positive blood group in male type 2 diabetic subjects (n=425).

Blood group (ABO-Rh positive)	N	%
'B'	192	45
'O'	154	36
'A'	51	12
'AB'	28	7

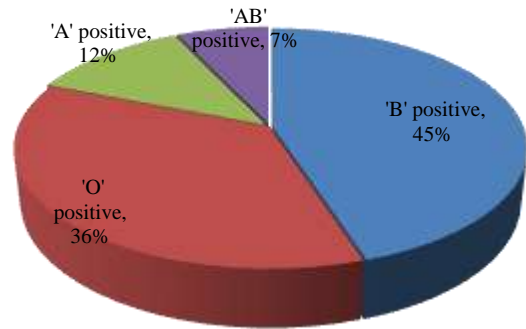


Figure 2: This figure shows the prevalence percentage of ABO-Rh positive blood groups among the male subjects suffering from type 2 diabetes mellitus.

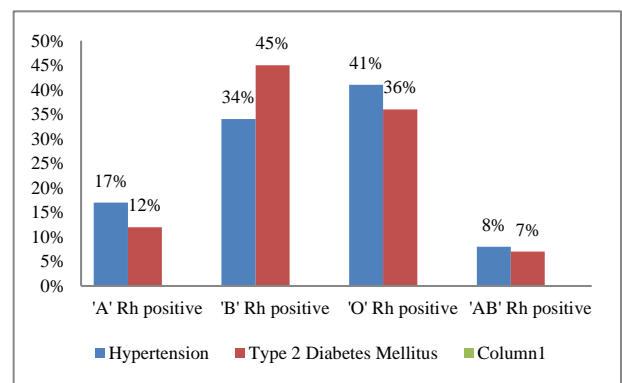


Figure 3: This figure shows the prevalence percentage of ABO-Rh positive blood groups among the male subjects suffering from hypertension and type 2 diabetes mellitus.

In the (Figure 3) it can be seen that 'B' Rh positive and 'O' Rh positive blood groups are more prevalent ones as compared to the rest of the ABO-Rh positive blood groups among the subjects suffering from hypertension or type 2 diabetes mellitus.

DISCUSSION

Genetics as evidenced by various research works plays an important role in the inheritance of different physiological mediators and it is in this regard that diseases like hypertension, diabetes mellitus and many others have a genetic predisposition. So, there lies a genetic mediation which links the components of blood pressure regulation or that of insulin regulation along with the ABO and Rh blood group systems. Many previous studies have tried to link some diseases to the blood group system. Some important examples instituting the same are the association of blood group 'O' with diseases like peptic ulcer and ischemic heart disease, association of blood group A with gastric cancer and association of blood group B with certain congenital maxillofacial abnormalities.¹⁰ The ABO blood group system as evidenced by studies is also associated with placental malaria infections¹¹ and is an important

predictor of national suicide rate as well as an important genetic marker.¹²

Many studies show significant association between the ABO blood group and diastolic blood pressure and say that those carrying the A allele such as blood groups 'A' or 'AB' were less likely to have high diastolic blood pressure than those of blood groups 'B' or 'O'. This finding, in conjunction with the lower frequency of the 'A' allele in African derived as compared to European-derived populations, suggested a potential link between the ABO system and hypertension.¹³ There are also studies from North-East India that show that blood group 'O' Rh positive is the most prevalent among both the hypertensive males and females and is followed by blood group 'B' Rh positive, then 'A' Rh positive and finally 'AB' Rh positive blood group.^{14,15} Susceptibility of a blood group to hypertension may also be determined in terms of the level of Von-Wille brand factor in a person's body as its normal range varies among individuals with different ABO blood groups. Lowest Von Wille brand antigen level is seen in blood group 'O' persons, followed by group 'A', then blood group 'B' and at last in blood group 'AB'. In blood group 'O' individuals also the factor VIII is about 25% less than normal which along with the decreased Von-Wille brand factor may be playing an important role in the predisposition of hypertension in blood group 'O' individuals as evidenced by previous researches as the low level of these blood clotting regulating proteins increases the risk of cardiovascular diseases, thrombo-embolic disorders and other vascular abnormalities.^{16,17} Some studies also say that the individuals carrying the 'B' blood group were more susceptible to hypertension as compared to blood group 'A' and 'O'. Whereas 'AB' blood group individuals are least susceptible to hypertension.¹⁸ There are also a plenty of studies which document otherwise. Some studies documented that the individuals of different blood groups were equally susceptible to different cardiovascular major risk factors whereas a few others show no crucial relationship in between the development of cardiovascular disease such as coronary heart disease and the association of ABO blood groups.^{19,20}

The association of diabetes mellitus with ABO blood group system has also been documented by many previous studies such as the one from Tokyo, Japan which shows that the persons belonging to blood group 'B' had an increased association with 2 diabetes mellitus as compared to other blood groups.²¹ Blood group 'B' is associated with alcohol drinking habits in diabetic patients as per a few studies and also many studies are in the favour that in blood group 'B' is associated with high incidence of type 2 diabetes whereas the blood groups 'A' and 'AB' were almost equally distributed in both diabetic and non-diabetic population.^{22,23} Also, studies have shown higher association of gestational diabetes mellitus with pregnant ladies belonging to blood groups 'B', 'O' and 'A' as compared to 'AB' blood group.²⁴ A few Indian origin studies have also shown that the blood

group 'B' and 'O' are more prevalent among type 2 diabetes mellitus individuals.²⁵ On the other hand, several investigators have also observed varying results. A number of studies from various parts of the Asian sub-continent have documented a higher occurrence of blood group 'O' among both the male and female individuals suffering from type 2 diabetes mellitus.²⁶ Also, a study from Pakistan documented that it is blood groups 'O' and 'AB' which are more in association with type 2 diabetes mellitus as compared to other ABO blood groups. The geographical and racial differences may be the possible reasons which lie at the core for these observed differences in blood group association with respective diseases as the genetic mediation of the components of the disease and its association with the markers of expression of ABO blood group antigens may be affected by the same.²⁷ Also, females belonging to blood groups 'O' and 'AB' of ABO blood group system and Rh positive blood group showed an increased risk of gestational diabetes mellitus as documented by some studies.²⁸ Also, some studies apart from reporting a higher fraction of blood group 'AB' among type 2 diabetic individuals as compared to controls have also reported lesser distinction of blood groups 'A' and 'B' as compared to normal subjects, equal distribution of blood group 'O' among both groups and even Rh negative blood type to be more common in the diabetics.²⁷ On the other hand there are also studies such as an Egyptian study suggesting the protective effect of blood group 'AB' against type 2 diabetes mellitus and hence documenting that blood group 'AB' is not commonly found among the type 2 diabetics.²⁹ Again, several studies have also documented a decreased association of blood group 'O' and type 2 diabetes mellitus and have cited the protective effect of the blood group 'O' in instituting lower levels of inflammatory mediators like factor VIII, Von-Wille brand factor complex, intercellular adhesion molecule-1, tumour necrosis factor-2 along with others to be the cause for its decreased association with the same.³⁰ Also, there was no difference in between the association of different blood groups among the diabetic population as cited by a study conducted in Algeria³¹ which is in accordance with some other researches which show no significant correlation of association of ABO blood groups and secretor status among diabetics as compared to controls.³² ABO-Rh blood group system is linked to specific molecules in association with type 2 diabetes mellitus as the ABO blood group antigen especially A and B antigens enhances the general body inflammatory state as evidenced by many previous studies as they promote genetic mediation of single nucleotide polymorphisms at the ABO locus which are linked with soluble intercellular adhesion molecule 1, E-selectin, P-selectin, tumor necrosis factor 2 along with other inflammatory markers which set up an acute phase response with increased hepatic production of C-reactive protein leading to insulin resistance in the liver, skeletal muscle, vascular endothelial tissue along with other sites of a human body and ultimately leading to the development and progression of type 2 diabetes mellitus.

^{33,34} It is worth noting that the search for disease-blood group association has often been criticized as studies on different populations have often failed to confirm initial reports. It is note-worthy yet there lies a large possibility that such inconsistencies are due to vastly different environments in study populations. In the British Caucassian population, the frequency of group 'A' is 42%, 'B' is 9%, 'AB' is 3% and 'O' is 46%, but there is racial variation in the frequencies. Also, sex distribution had no significant association with the blood groups. Many studies say that blood group 'O' is the most common blood group in India. More than 60% of the population in India has blood group 'A' and 'O', followed by blood group 'B' and finally by blood group 'AB'. A nation such as India is not only geographically large and extensive but also is gifted with a lot of diversity in race, religion, culture, creed and ethnicity. So, in India diversity has been observed in the distribution of blood groups in population within the country and it is evidenced by some of the studies performed in different geographical parts such as in South India and Jammu and Kashmir to name a few. The study from South India documented the blood group 'O' to be the commonest, followed by blood group 'B', then blood group 'A' and finally blood group 'AB'.³⁵ Similarly the study from Jammu and Kashmir also showed 'O' to be commonest among ABO group in their population.³⁶ The reason for the lack of association as shown by some studies between ABO-Rh blood groups and hypertension and type 2 diabetes mellitus in different parts of the world might be the sample size, age and gender distribution, environmental factors and racial diversity among other factors which may affect the distribution of different blood groups and incidence of the respective diseases. The finding of disease-blood group associations enlightens the fact that there lies an existence of significant physiological differences among individuals of different blood groups and so it is possible that it is not the presence of a given blood type but it is actually the absence of the protective effect of other alleles that is responsible for disease development and hence further evidencing the fact that disease-blood group associations such as the one with ABO-Rh blood groups with hypertension and type 2 diabetes mellitus really do exist.

In current study the small sample size was a limitation as due to the limited number of the participants, this study was conducted in a measured design. Also, in this study only male subjects were included so there is a prospect of performing a similar study with female subjects in Deoghar. Also, there was a nation-wide lock down in whole of India as like the rest of the world due to COVID-19 pandemic which lasted for most of the 2020 year which also affected the study in terms of increasing the sample size. Also, there is a prospect of performing a large scale study with both ABO-Rh positive and negative blood groups among both male and female subjects suffering from hypertension and type 2 diabetes mellitus in different parts of our country as it will give

more insight into the relationship between different blood groups in relation to hypertension and type 2 diabetes mellitus. Also, evaluation of the etiological relationship of blood groups with that of hypertension and type 2 diabetes mellitus is important as this study has shown that in certain blood groups the prevalence of hypertension and type 2 diabetes mellitus is more common and so the persons belonging to those blood groups should take adequate precautions since their childhood against these co-morbidities.

CONCLUSION

This study has shown that the blood group 'O' Rh positive is the most prevalent one followed by 'B' Rh positive which is followed by 'A' Rh positive and lastly by 'AB' Rh positive blood group among the hypertensive urban population of Deoghar. Also, blood group 'B' Rh positive is the most prevalent one followed by 'O' Rh positive which in turn is followed by 'A' Rh positive and finally by 'AB' Rh positive blood group among the type 2 diabetic urban population of Deoghar. Thus, this study shows that blood groups 'O' Rh positive and 'B' Rh positive are more prevalent as compared to blood groups 'A' Rh positive and 'AB' Rh positive among the urban male population in relation to hypertension and type 2 diabetes mellitus in Deoghar, Jharkhand. The findings of this study suggest that physicians should be more careful and they should closely monitor the individuals with certain blood groups as the individuals belonging to those blood groups are more prone to develop the respective diseases. It may also help to understand the genetic relationships among these blood groups as well as development of hypertension and type 2 diabetes mellitus as further research takes place in this field and thus may assist in finding treatment of these diseases at even the genetic level.

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