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Frequency of ABO and Rh Blood Groups and Their Association With Essential Hypertension

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ABSTRACT

The ABO and Rh systems are the blood groups most often recorded in clinical practice, and because they are cheap to determine they are also among the most frequently tested for association with common disease. Essential hypertension, the form of raised blood pressure with no single identifiable cause, has repeatedly been examined from this angle, with results that are scattered and often contradictory. This narrative review asks what the published literature actually supports. It covers the molecular basis of the two systems, the distribution of the groups between populations, the better-documented links between ABO and vascular and thrombotic disease, and the genetic and epidemiological evidence on blood pressure. The review reports no new data and no local frequencies. A plausible biological route exists for ABO, through von Willebrand factor and endothelial adhesion molecules, while for Rh the route is speculative. Genome-wide studies of blood pressure have not highlighted the ABO locus, and the direct hypertension literature consists largely of small, single-site comparisons that are vulnerable to population stratification, confounding and selective reporting. The balance of the evidence is that any association between blood group and essential hypertension is unproven, probably small if present, and not a basis for screening or counselling. The review closes with the design features a convincing study would need.

Keywords: ABO blood group; Rh blood group; Essential hypertension; Population stratification; Cardiovascular risk; Narrative review

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Article Class: Narrative Review

1. Introduction

Few laboratory results are as familiar as a person's blood group. ABO and Rh type are recorded at birth, at the blood bank, before surgery and in antenatal care, and

the information costs almost nothing to collect once the sample is in hand. That convenience has made the blood groups a favourite candidate for studies of disease association for well over a century, and the



literature is correspondingly large (1). Some of those associations are firm. Others have drifted from paper to paper without ever being tested properly.

Essential hypertension sits in the second category more often than the first. It is the commonest form of raised blood pressure, defined by exclusion, since no single secondary cause can be found (2). It is a leading contributor to the global burden of cardiovascular disease (3, 4), and in India, as elsewhere, many affected adults are unaware of their status (5). An inexpensive marker of risk would be welcome, and a comparison of blood group frequencies between people with and without hypertension is an easy project for a laboratory that already holds the typing records.

This article reviews what the published literature says about that comparison. It is written in response to a title that suggests a local frequency study, but it reports no local data of any kind: no counts, no percentages, and no claim that the authors collected or tested anything. Instead it asks what an informed reader should believe about the link between ABO and Rh groups and essential hypertension, and why the evidence is as thin as it is. The aim is a fair account of what is known, what is plausible and what is simply repeated.

2. Literature Review

2.1 The ABO and Rh Systems

The ABO system is controlled by a single gene whose product is a glycosyltransferase. The A and B alleles differ by a handful of amino acid substitutions that change which sugar the enzyme adds to a precursor carbohydrate chain, while the common O allele carries a small deletion that shifts the reading frame and leaves no functional enzyme (6). The result is that group A cells carry one terminal sugar, group B cells another, and

group O cells neither. Because the antigens are carbohydrates attached to proteins and lipids, they appear on many cell types beyond the red cell, including vascular endothelium and platelets, and on circulating plasma proteins (1, 7).

Rh is a different kind of system. Its antigens are proteins, encoded by two closely related genes, RHD and RHCE, and they sit in the red cell membrane as part of a larger complex that may help transport ammonium (8, 9, 10). The familiar label of Rh positive or negative refers to the presence or absence of the D antigen, and in many populations D negativity arises from deletion of the whole RHD gene (11). Nothing in this literature points toward a direct effect of Rh on blood pressure. Table 1 sets the two systems side by side.

Table 1. The ABO and Rh systems compared.

Feature	ABO	Rh
Genetic basis	One gene encoding a glycosyltransferase (6)	Two closely related genes, RHD and RHCE (8, 11)
Nature of antigen	Carbohydrate chains on proteins and lipids	Membrane proteins in a larger complex (9)
Where expressed	Red cells, endothelium, platelets, plasma proteins (1)	Essentially red cells
Functional hints	Shapes circulating adhesion and clotting proteins (12)	Ammonium and gas transport suggested (10)
Population spread	Wide and uneven (13)	Wide and uneven (13)

Note: Qualitative summary of the cited literature. Frequencies are deliberately omitted because they differ between populations.

2.2 Antigens Beyond the Red Cell

ABO attracts more interest than Rh in vascular research because its antigens are not confined to red cells. Plasma von Willebrand factor carries ABO determinants, and people of group O tend



to have lower circulating levels of the factor, and of factor VIII, than people of other groups (12). The antigens appear to influence how quickly the protein is cleared (14).

Genetic studies reinforced the point. Genome-wide analyses found that variation at the ABO locus is the dominant influence on soluble intercellular adhesion molecule 1 in women (15), and a major determinant of soluble E-selectin and P-selectin (16, 17). These are markers rather than mechanisms, and a shift in a circulating level does not itself show a shift in disease. They do show that ABO status leaves a measurable imprint on the vessel wall, which is where hypertension does its long-term damage.

2.3 Why Blood Group Frequencies Differ

Group frequencies differ between communities: surveys of large donor populations within a single country already show clear differences between ethnic groups (13). The ABO polymorphism is also very old, shared across primate lineages, which suggests that balancing selection has maintained it (18).

Infection is the most discussed source of that selection. ABO glycosyltransferase variation has been linked to susceptibility to severe falciparum malaria (19), and group O protection is attributed to reduced rosetting of infected red cells (20). The lesson here is practical. If group frequencies track ancestry and local disease history, and blood pressure and its determinants also differ between populations, a crude comparison of blood groups between two unlike samples can produce an association that has nothing to do with the blood group. An association that vanishes once ancestry is accounted for was never an association with the blood group itself.

2.4 Blood Groups and Cardiovascular Disease

An older body of work examined ischaemic heart disease. A study of British men reported a weak association between ABO group and ischaemic heart disease (21), and a later systematic review of the vascular literature found that non-O groups were associated with a higher risk of coronary events, with a stronger signal for venous thrombosis (22). Two large prospective cohorts of health professionals reached a similar conclusion for coronary disease (23), and a meta-analysis ranked non-O blood type among the commonest genetic risk factors for venous thromboembolism (24).

Genetic data pointed the same way. The ABO locus appeared among the loci associated with coronary disease in large genome-wide studies (25, 26). Overviews describe the evidence as consistent in direction but modest in size, with the von Willebrand factor pathway as the favoured explanation (27). Blood group findings turn up for many other conditions too, type 2 diabetes among them (28), and each needs replication before it is believed. This is the context in which hypertension is usually brought in: if ABO influences vascular outcomes, perhaps it influences blood pressure too. The inference is natural, but it is an inference, and a different outcome needs its own evidence.

2.5 Essential Hypertension: Burden, Causes and Measurement

Blood pressure and vascular risk are related continuously, with no clear threshold (29), although guidelines need a cut-off and those have moved over time (30). Essential hypertension has no single cause. Reviews of its pathogenesis stress the interplay of renal sodium handling, the sympathetic nervous system, the renin-angiotensin system, vascular structure and inherited susceptibility (2,



31). Rare monogenic forms mostly involve salt handling in the kidney (32) but explain little of the common disorder. Dietary sodium and potassium show a consistent relationship with blood pressure across populations (33), and vascular inflammation has attracted growing attention (34).

Two points follow. First, a study of blood group and hypertension must deal with an outcome driven by age, adiposity, diet and family history, among other factors. Second, the genetic contribution is spread across many loci of small effect, so that any single polymorphism is expected to account for little. Small differences of this kind are easy to dismiss, yet they are the ones large studies exist to detect.

3. Materials and Methods

3.1 Scope and Question

This is a narrative review. Its question is whether published evidence supports an association between ABO or Rh blood groups and essential hypertension, and if so how large and how reliable it appears to be. We included material on the molecular biology of the two systems, on population differences, on vascular disease associations, and on the genetics and epidemiology of blood pressure, since each bears on the plausibility of the main question.

3.2 Literature Assembly

No formal systematic search was carried out and no protocol was registered. Sources were found by reading and by following references in key articles, and were chosen to illustrate the main lines of evidence rather than to count every study, which carries a risk of selective citation (35). We cite only work published up to 2015, the year of this issue, and favour large studies, systematic reviews and authoritative guidelines over single-centre reports.

Small single-site comparisons of blood group in people with and without hypertension appear in the regional literature of several countries. We do not cite them individually, because we could not verify their details against the original publications, and we describe their general character instead.

3.3 Appraisal Framework

Each line of evidence was read against a small set of questions drawn from reporting guidance for observational and genetic association studies (36, 37). These concern who was sampled, whether ancestry and confounders were handled, how hypertension was defined, whether analyses were specified beforehand, and whether the methods were reported completely. Table 2 lists the questions and the weaknesses most often found. None of these checks is difficult, but each is easy to skip when a result looks tidy.

4. Results

4.1 What the Direct Evidence Looks Like

The direct literature on blood group and hypertension has a recognisable shape. Typical reports compare the distribution of ABO and Rh groups among hospital patients with hypertension and a comparison group, often drawn from blood donors or other patients, and test for a difference using a simple chi-square comparison. Different studies single out different groups, and some report no difference at all. This is why the same blood group can look important in one report and irrelevant in the next. Because the studies differ in population, definition and comparison group, their disagreement cannot be taken as evidence that the true effect is heterogeneous. The point is not that a study is poor, only that its result travels less far than its abstract suggests.

**Table 2.** Appraisal questions applied to each blood group and blood pressure report.

Question	Why it matters	Typical weakness
Who was sampled?	Selection can create or hide a link (36)	Hospital or donor groups only
Was ancestry considered?	Allele and disease rates both vary (38)	Mixed communities pooled
Were confounders handled?	Age, weight, salt and kin matter (2, 33)	Crude comparison only
How was hypertension defined?	Thresholds have changed over time (30)	One reading, or none stated
Were methods reported fully?	Allows replication (37)	Typing method not described

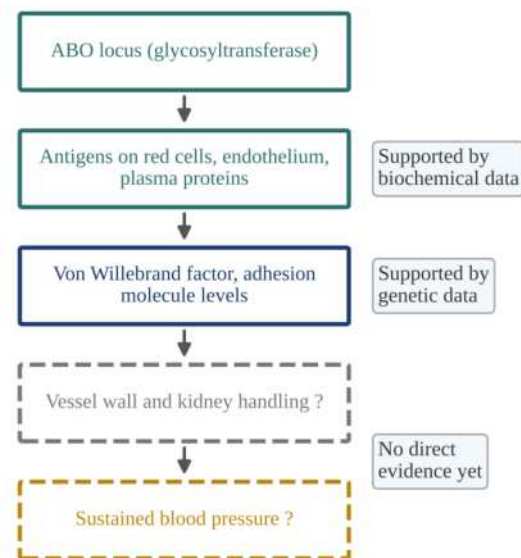
Note: Questions are those commonly recommended for observational and genetic association studies; they were not scored.

Several features make these reports hard to interpret. Samples are small, and the comparison group is rarely matched for age, sex or body weight. Ancestry, region and community are rarely described, although they matter if group frequencies vary within a catchment area. Many groups and subgroups are compared, and those reaching nominal significance tend to be the ones highlighted. A positive finding in a small sample is therefore more likely to be an artefact than a discovery (39, 40). A clinician reading such a paper needs one answer above all: would this change anything I do?

4.2 Candidate Routes From Blood Group to Blood Pressure

For a causal link to exist, something must connect the antigen to the vessel or the kidney. [Figure 1](#) sketches the steps that would be required, from the ABO locus to blood pressure. The first are the best documented: the locus shapes von Willebrand factor and adhesion molecule levels (12, 15, 16). The later steps, from

those markers to a sustained rise in blood pressure, have no supporting data.

**Figure 1.** From the ABO locus to blood pressure: a chain of possible steps, each needing its own evidence (schematic, not data).

[Table 3](#) gathers the proposed routes and shows how uneven the support is. Vascular inflammation is a credible theme in hypertension research (34), but no blood group specific work connects it to ABO, and shared infection history (19, 20) is more remote still. The last row, chance and population structure, deserves equal billing, because it explains many small positive reports without any biology at all.

4.3 What Genetic Studies of Blood Pressure Show

If ABO had a sizeable effect on blood pressure, large genome-wide studies would be expected to find it. The early scans of blood pressure and hypertension in tens of thousands of people identified a series of loci, each with a small effect (41, 42). A larger consortium later increased the number of known loci and showed that they were relevant to cardiovascular outcomes (43). To our reading of those reports, ABO was not among the loci identified, although it did appear in



genome-wide work on coronary disease (25, 26).

Table 3. Routes proposed to link blood group with blood pressure.

Route	Current support	Main difficulty
Von Willebrand factor and factor VIII	Well documented for ABO (12, 14)	Link to pressure itself unshown
Soluble adhesion molecules	Genetic evidence for ABO (15, 16, 17)	Marker, not proven cause
Vascular inflammation	Plausible in hypertension generally (34)	No blood group specific data
Rh complex transport role	Speculative (10)	No clear mechanism
Chance and structure	Fits many small reports (38, 39)	Cannot be excluded easily

Note: Support is the authors' qualitative reading of the cited literature, not a graded score.

That contrast is informative. This does not exclude a small effect, since the scans were powered for common variants of modest size, but it suggests that any effect is smaller than those of the loci that were found, which are themselves small. Read this way, a null result from a small sample says very little.

Mendelian randomisation offers a more direct causal test, using genetic variants as instruments for exposures that are otherwise confounded (44, 45). Blood group is fixed at conception and cannot be changed by disease, which is attractive, but the method needs large samples and careful thought about pleiotropy at a locus as biologically busy as ABO.

4.4 Confounding, Stratification and Selective Reporting

Figure 2 shows how an apparent association can arise without any causal effect of blood group. Ancestry influences allele frequencies, and it may also influence blood pressure through diet,

environment and other inherited factors. If cases and comparison subjects are drawn from slightly different ancestral backgrounds, the blood group will seem to be linked to hypertension. This is population stratification, and it is a well-recognised source of spurious genetic association (38). In a similar way, a study drawn only from patients at one hospital selects people who share more than their diagnosis.

A further difficulty is the pattern of publication. Genetic association studies have a history of initial positive findings that fail to replicate (40), and where analyses are many and prior hypotheses few, the published record is likely to over-represent chance results (39). Causal reasoning in epidemiology asks for more than a statistical association (46), and in this literature the evidence for the rest of the chain is limited. These cautions apply to any inexpensive marker, not only to blood group.

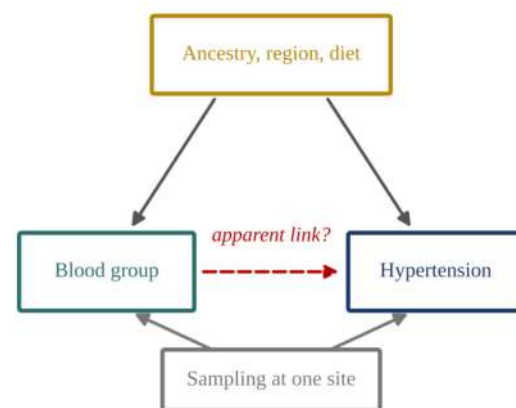


Figure 2. Causal diagram showing how ancestry and sampling could produce an apparent association (schematic, not data).

Figure 3 pulls the preceding sections into a qualitative matrix, meant as a reading aid and not a measurement. Venous thrombosis and coronary disease are far better supported than hypertension.



	Biology	Genetics	Cohorts	Small series
Venous thrombosis	good	good	good	some
Coronary disease	some	good	good	some
Adhesion markers	good	good	none	none
Hypertension	weak	none	weak	some

Strength of available evidence (schematic, not data)

Figure 3. Qualitative evidence matrix for blood group and vascular outcomes (schematic, not data).

5. Discussion

5.1 Interpretation

The overall picture is of a plausible biology at one end and weak epidemiology at the other. ABO status is linked to vascular disease, and there are reasonable mechanisms through which that could occur. It does not follow that blood pressure shares the link. The genetic evidence from blood pressure scans does not highlight the locus, the Rh system has no credible route, and the direct literature is dominated by small studies with predictable weaknesses. Reviews of this kind are more useful when they say where the evidence stops than when they smooth it over.

It is worth saying plainly what this review does not conclude. It does not conclude that there is no association, only that none has been shown convincingly. A small effect of the kind seen for coronary disease would be hard to detect in a hospital series of the usual size, so its absence from the published record would not be surprising either way. Nor does it conclude that blood group is irrelevant to cardiovascular health. The matter is unsettled, and the amount of uncertainty is itself a finding.

For readers in clinical or laboratory practice, the implication is straightforward. Blood group is not a recognised risk factor for essential hypertension and is not part of

any guideline for assessing it (30), and nothing reviewed here supports using it to screen or counsel individuals. Blood pressure itself should be measured and interpreted by the established methods. It is a habit worth keeping even when the answer seems obvious.

5.2 Limitations

This review has the limitations of its kind. The literature was not searched systematically, selection was by judgement, and relevant work may have been missed. The many small regional studies are described in general terms only, so a reader wanting effect sizes will not find them here. The mechanistic material comes partly from other outcomes and is not direct evidence about blood pressure. The review also reports no local frequencies, and anyone planning a study in a particular district would still need to describe their own population.

5.3 Future Work

A study that could move the field would be large, defined in advance and honest about its comparison group. It would record age, sex, body mass and family history, define hypertension by a stated protocol with repeated readings, and treat blood pressure as a continuous outcome as well as a binary one. It would describe ancestry or control for it with genetic markers, state its typing method, and report results for all ABO and Rh groups whether or not they were significant, with a plan for replication (37, 39). A hypothesis that can be written down in advance is far harder to bend afterwards.

Beyond new cohorts, existing genetic consortia already hold both blood pressure and ABO information, and a causal analysis could be run without new sample collection (45). Studies of von Willebrand factor and soluble adhesion molecules within hypertensive patients would show



whether the first steps in [Figure 1](#) connect to the later ones. Nothing in this reading argues against looking; it argues for looking properly.

6. Conclusion

The ABO and Rh blood groups are easy to measure, biologically interesting and demonstrably linked to some vascular outcomes. The evidence that they are linked to essential hypertension is much weaker. What exists is a collection of small, inconsistent, single-site comparisons that are open to stratification, confounding and selective reporting, set against genetic data that do not single out the locus. We therefore regard the association as unproven and, if real, probably small. That is a modest claim, and it is the one the literature will currently bear.

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9. Conflict of Interest

The authors declare no conflict of interest.

10. Author Contributions

P.T. conceived the review and wrote the sections on blood group biology. D.K. wrote the sections on hypertension and its measurement. P.C. wrote the sections on genetic evidence and study design. All authors revised the manuscript and approved the final version.

11. Ethics Statement

This is a review of published literature. No human participants or animals were involved and no ethical approval was

required.

12. Data Availability

No new data were generated. All sources are cited in the reference list.

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