BLOOD TYPE EFFECT ON COVID-19 INFECTION AND TOOTH MOVEMENT

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ABSTRACT

Introduction: The objective of this study was to explore the influence of ABO blood type on COVID-19 infection rate. Discovered relationships may uncover whether genetic makeup may affect treatments and such information could be related to orthodontic tooth movements.

Methods: The PubMed database was searched using the terms: ABO Blood Group System; Blood-Group System, ABO; System, ABO Blood-Group; H Blood Group System; H Blood Group; Blood Group, H; ABH Blood Group; Blood Group, ABH; Blood Group H Type 1 Antigen; ABO Factors; Factors, ABO. Also included, were studies of ABO blood type and COVID infection or outcomes. Opinion pieces, animal studies, in-vitro studies, studies using blood other than ABO, and pre-2000 papers were excluded, as were studies that were not published in or translated to English. Of the included studies, the references were manually screened to identify additional qualified studies. Two independent reviewers reviewed the initial batch of reports to select the appropriate publications. To resolve conflicts, they met to discuss for a consensus. Studies were appraised by the Joanna Briggs Institute appraisal index. For the meta-analysis, studies which used odds ratio in their statistical analysis and COVID-19 infection as an outcome were included. Outcomes were analyzed using Forest Plots.

Results: Overall, this systematic review included 39 studies. 19 studies were cohort (2 prospective and 17 retrospective), 16 retrospective case control, and 4 were systematic reviews or meta-analysis. 31 studies reported a relationship between ABO blood type and COVID infection rates and 5 studies found no relationship. For the meta-analysis, 13 studies were included and analyzed. The estimated frequency of COVID-19 infection

in terms of ABO blood groups and the overall effect size between blood groups was calculated with 95% confidence interval. The effect size of COVID-19 infection for blood group O versus the other blood groups was estimated as 0.174 (95% CI, o.o86-0.261) p<0.001. The effect size of COVID-19 infection for blood group A versus non-A was estimated as -0.174 (95% CI, -o.248- -0.100) p<0.001. The effect size of COVID-19 infection for blood group B versus non-B was estimated as -0.010 (95% CI, -0.107-0.086) p=0.831. The effect size of COVID-19 infection for blood group AB versus non-AB was estimated as -0.140 (95% CI, -o.344-0.064) p=0.179.

Conclusion: This meta-analysis indicates individuals with type O blood may be less susceptible to COVID-19 infection while those with type A blood may be more susceptible. Numerous studies, however, were not methodologically strong, as they had small sample size or suffered selection bias. Furthermore, no randomized controlled trials to determine causal relationships were found. Clearly this is understandable, given the speed with which the studies needed to be published. Despite such limitation, these findings have important implications for orthodontics because it may indicate that those with variants of Type A blood are more prone to inflammation, as orthodontic tooth movement is facilitated by the inflammatory responses of periodontal tissues.

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CHAPTER 1

INTRODUCTION

Clinical studies with human subjects are known to yield varied results. Investigators are often confounded as they cannot replicate previous studies (Tuncay, 2015). In fact, it has been stated that clinical science is facing a reproducibility crisis (Feilden, 2017). It is uncomfortable to report to evidence-based health care establishments that much of the collected data cannot be convincingly substantiated. One study, for example, attempted to reproduce five landmark cancer studies and was only able to confirm two (Feilden, 2017). Another report, published in Nature, states that over 70% of scientists have attempted, but were unable to replicate another researcher's experiments (Feilden, 2017).

One possible explanation for this dilemma of inconsistent results could be, subjects were not properly genetically matched. Clinical studies must often ignore or overlook the inherent fact that experimental and control groups are genetically heterogeneous. Hence, investigations conducted on heterogenous samples are destined to yield inconsistent or irreproducible results. Conclusions will always be that there is no difference between the two groups, when there is, or vice versa. Ill-matched samples will naturally skew the data (Tuncay, 2015). Translation of imprecise results ought not be translated to human subjects; yet, it has long been tolerated. For example, for decades, the biological and environmental differences between males and females were ignored. Results of studies with solely male subjects were indiscriminately applied to women (Liu,

2016). Such practice of not conducting studies on women, has greatly delayed the understanding of women's reactions to disease and medications (Liu, 2016). Upon appointment of Bernadine Healy as director of the NIH, both male and female subjects were required to be included in a study for it to be funded (U.S. Department of Health and Human Services, 2017). It is now known, some diseases disproportionately affect women, women may have differing symptoms, and women respond to treatment differently than men (Liu, 2016). Awareness of gender difference has been an excellent first step. Assessment of genetic gender differences is similar to certain cancer treatments that utilize genetic assessment for targeted therapies. This field of study is known as cancer genomics, and the goal is to destroy cancer cells while leaving healthy ones untouched (National Cancer Institute, 2017).

If this one-size-fits-all practice could be eliminated and replaced by proper identification of the make of different humans, predictions of treatment outcomes would be done with elevated certainty. Some work has been done to study the link between ethnicity-related genetic markers and certain diseases such as cancer (Smigal, 2009; Gilliland, 1997; Jing, 2014; Quiñones, 1999) and diabetes, (Marron, 1997; Waters, 2010) as well as, post-operative pain management (Somogyi, 2016). Other diseases such as cystic fibrosis (Kerem, 1994) and sickle cell anemia (Mohammed, 2006) possess well-known links with genetic markers related to ethnicity. With the advent of resources such as 23andme and the unveiling of the human genome, the clinical application and understanding genetic variability is becoming more and more feasible and promising (Cavalli-Sforza, 2005).

In dentistry, studies have been conducted to assess the risk factors in periodontitis as related to ABO blood groups (Kaslick, 1971). Similar studies were also done on denture plaque accumulation and denture stomatitis (Nikawa, 1991). In both medicine and dentistry, existing reports on blood type are mainly focused on disease and complications, rather than treatment outcomes. To our knowledge, there are no published reports of blood type effects on orthodontic treatment. A body of work on this topic could allow orthodontists to revolutionize treatment planning. We posit, evidence-based consideration of patients' genetics could yield more predictable results. The aim of this study is to specifically investigate whether patients' ABO blood types affect likelihood of COVID-19 infection and severity and relate these findings to tooth movement.

CHAPTER 2

REVIEW OF THE LITERATURE

2.1 Biology of Tooth Movement

A number of studies have investigated the biological mechanisms of tooth movement in hopes of shortening orthodontic treatment time. Arguably, orthodontic treatment takes longer than any other dental treatment. Orthodontic treatment is a process; and is long. It would benefit clinicians and patients alike, to increase treatment efficiency.

It is well-known, best results can only be achieved with ideal patient compliance throughout the treatment period. Yet, patient burnout is common, and compliance with hygiene, attendance, and elastics decrease with prolonged treatment (Brezniack, 1989). Orthodontic treatment commonly lasts 18-24 months, sometimes longer, and patient cooperation diminishes after 6-9 months (Brezniack, 1989). This endangers the oral health of young patients, and potentially leads to compromised results (Brezniack, 1989). Patients who remain in treatment longer, are at risk for white spot lesions, root resorption, caries, and gingival inflammation (Pinto, 2018). Furthermore, psychologically, extended treatment time could lead to frustration and a negative view of dentistry at a formative age (Brezniack, 1989).

The biological basis of orthodontic tooth movement is now better understood, with abundant data, mostly through animal studies (Proffit, 2019). Notably, the differential turnover rate, remodeling of periodontal ligament and alveolar bone, are better known

(Graber, 2017). On the resorptive surface, towards which the tooth is moving, there are more osteoclasts present while on the depository surface, where the tooth is moving away, there are more osteoblasts present (Graber, 2017).

It was discovered by Tuncay et al. that orthodontic tooth movement is an inflammatory process within the periodontal tissues (Tuncay, 2006). Cytokines, which are also known as inflammatory mediators and calcitonin gene-related peptide, in addition to substance P, are important factors in remodeling the PDL (Meikle, 2006). Describing orthodontic tooth movement as simply inflammatory is an understatement. Rather, it is better characterized as wound healing: a process which consists of a continuous cycle of inflammation and repair. Some describe it as an "exaggerated form of normal physiological turnover" (Meikle, 2006).

Orthodontic tooth movement is unique because it creates an aseptic inflammatory response, unlike other types of inflammation in the body that are typically precipitated by some sort of infection, injury, or toxin (Li, 2018). When mechanical forces are applied to the teeth, areas of compression and tension created in the periodontal ligament space. Subsequently, nerve endings are distorted and they release substance P and CGRP (Li, 2018). These neurotransmitters affect the vascular endothelial cells. In turn, they activate the endothelium (Li, 2018). Later, leukocytes, monocytes, and macrophages are recruited to the periodontal ligament. This is the acute inflammation stage. After a few days, tissue remodeling and soon after, the chronic inflammation stage is entered (Li, 2018). This proliferative process involves fibroblasts, endothelial cells, osteoblasts and osteoclasts (Li, 2018). A plethora of inflammatory factors are released including: cytokine IL-1B, IL-6,

IL10, Nitric Oxide, TNF-a, TGF-B, macrophage colony-stimulating factor, prostaglandins, OPG, and RANKL (Li, 2018).

Interestingly, compression and tension sites are associated with separate mediators. In compression sites, more COX-2 is found, which allows for the production of prostaglandins (especially PGE2) (Li, 2018). These act on osteoclasts, increasing cAMP and enhancing resorptive ability (Li, 2018). PGE2 stimulates osteoblast differentiation and increases the production of RANKL and OPG (Li, 2018). This prompts osteoclast differentiation and bone resorption. Importantly, compression also induces the production of nitric oxide which allows for inflammation-induced bone resorption (Li, 2018).

Meanwhile, on the tension side, alveolar bone deposition is occurring and increased numbers of osteoblasts are seen (Li, 2018). The present nitric oxide mediates bone formation and IL-10 increases. OPG is increased and RANKL is decreased (Li, 2018). Osteoclast formation and activity declines. Overall, tooth movement occurs once necrotic tissue is removed by osteoclasts and the osteoblasts create new bone with new periodontal fibers (Li, 2018).

Orthodontic tooth movement happens by the application of prolonged forces to the teeth. Such application is theorized to create piezoelectricity. It is conjectured that the organic crystals within the PDL produce a flow of electrons, as the crystal structure is deformed (Proffit, 2019). Interestingly, while the force is sustained the structure is stable and no further flow of electrons occurs. Later, when the force is released, a reverse flow of electrons is observed. Sustained force, such as the force used to create orthodontic movement is not thought to produce stress-generating signals. Some have attempted to use

this understanding of piezoelectricity to test if vibrations can accelerate tooth movement, with little luck (Proffit, 2019).

The pressure-tension theory, however, describes chemical signals as the main impetus for tooth movement. Pressure against a tooth compresses the PDL in some areas and stretches it in other areas. This causes the release of chemical messengers such as cytokines and prostaglandins, along with alterations in blood flow in the areas of compression and tension (Proffit, 2019). This school of thought hypothesizes that tooth movement occurs in three stages: initial compression of tissues and changes in blood flow, release of chemical messengers, and activation of cells (Proffit, 2019).

2.2 Methods to Shorten Orthodontic Treatment Time

As stated earlier, substantial work has been done to understand the biology of tooth movement, in the hope to shorten orthodontic treatment time. All were left with marginal success. For example, some have advocated that corticotomy, where shallow perforations are made in the cortical alveolar bone shortly before orthodontic tooth movement, has resulted in faster orthodontic treatment (Kole, 1959). There are several techniques based on this principle such as periodontal ligament distraction and dentoalveolar distraction where bone is surgically reduced to facilitate rapid canine retraction in premolar extraction patients (Hoogeveen, 2014). The supposedly more rapid tooth movement has been said to be based on a local increase in metabolism and transient osteopenia (Frost, 1983; Figueroa, 2005; Yaffe, 1994; Rodan, 2021; Davidovitch, 1980). A systematic review conducted by

Hogeveen et al., however, found that there is a limited level of evidence supporting that surgically assisted orthodontic treatment significantly reduces treatment time in comparison with conventional orthodontic treatment (Hoogeveen, 2014). Moreover, no clinical studies have properly addressed to the long term stability of such treatment (Hoogeveen, 2014).

Even magnets and electromagnetic fields have been explored to aid in tooth movement. It has been suggested that pulsed electromagnetic fields can improve the rate of orthodontic tooth movement due to a change in membrane permeability, which allows for an increased flow of calcium, sodium, and potassium ions across the cell membrane. Presumably, this affects the activity of intracellular cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (Rodan, 2021; Davidovitch, 1980; Davidovitch, 1980). Some studies have also examined the effects of rare earth magnets to apply mechanical forces for open bite closure, palatal expansion, or molar distalization (Vadimon, 1989; Graber, 1988; Vardimon, 1989; Vardimon, 1991; Sandler, 1991; Darendeliler, 1993). Unfortunately, most of these studies were limited to animal models thus, long term stability is unknown. Kevin O'Brien, a leader in the field of orthodontics, along with many others, often emphasizes the fact that the findings of animal studies do not readily transfer to human clinical treatment (O'Brien, 2020).

2.3 Individual Patient Characteristics in Orthodontics

Our study takes a different approach and examines the composition of the body rather than external factors. The modern view of orthodontics is that nature contends

with the orthodontist trying to achieve perfection. Failures in treatment are typically the result of poor treatment response rather than inadequate treatment. It is fully possible for two patients to receive the same treatment and respond completely differently. Thus, patients can be categorized as "responders" or "non-responders" to treatment procedures (Graber, 2017). If this is the favored argument, then it is unreasonable to spend much time and energy to explore if external factors can affect tooth movement while internal factors are largely ignored. Individual patient characteristics and how they affect tooth movement must be better understood. This study is the first step.

Ethnicity is an individual patient characteristic that appears to influence orthodontic diagnosis, mechanotherapy, and orthodontic treatment time. One such example is skeletal classification. It varies among different ethnic groups (Graber, 2017). In particular, Asian populations have been shown to exhibit a higher prevalence of the Class III malocclusion phenotype (Lew, 1993; Tang, 1994; Woon, 1989; Soh, 2005; Soh, 2005). Genetic studies in this population have linked it to certain locations of genetic loci. They may influence the Class III trait on several chromosomes and multiple loci, and candidate genes have been connected to this phenotype (Graber, 2017).

Interestingly, bone density varies between among the ethnic groups. It has been reported that African American women show higher bone mineral density than white American women (Conradie, 2014). Clinically, people of African ancestry have a lower incidence of fragility fractures than those of European ancestry (Conradie, 2014). Similarly, studies of long bones have shown that there is increased cortical and trabecular thickness in the long bones of Chinese women compared to Caucasian women (Wang,

2009). Racial differences in the biomechanical aspects of bone are continuing to be illuminated. One can be optimistic that such studies could prove to be essential in understanding the biology of tooth movement among different ethnicities. Variations between racial groups have also been found in the maxillary sinus volumes. One study in particular found that European subjects had larger volumes than Zulu subjects (Fernandes, 2004).

Furthermore, in cephalometric analysis, it has been acknowledged that there is variation in what is considered normal between different ethnicities. Crafted by Downs, Steiner, and Ricketts, the initial measurements were based on Caucasian subjects only, and were not as useful for other ethnicities (Zylinski, 1992). Much effort has been dedicated to determining the average values of certain points such as SNA, SNB, ANB, and FH-MP, among others, for African-American, Asian, White, and Hispanic patients (Turley, 2015; Wu, 2007; Lew, 1992; Io, 2007; Alcade, 2000; Miyajima, 1996; Uesato, 1978; Hwang, 2002; Park, 1989; Evanko, 1997). All these ethnicities vary considerably in the average cephalometric measurements. This must be taken into consideration, as the orthodontic clinician crafts the goals of treatment. Similarly, in soft tissue analysis there exists variation that greatly affects treatment planning. One specific example is Ricketts' esthetic line measurement. It is a line drawn from the tip of the chin to the tip of the nose. Then the distance from the upper and lower lips to this line are measured. In Caucasians, Ricketts stated, that the upper lip should be 4 mm behind the line while the lower lip should be 2 mm behind the line (Ricketts, 1982). In African Americans, however, it was shown that the upper lip is more commonly 0.33 mm ahead of the

esthetic line, while the lower lip is 2 mm ahead of the esthetic line (Sushner, 1977). The esthetic line is one simple example of a factor crucial in treatment planning that greatly differs between the ethnic groups. These differences support the fact that findings in white patients cannot be easily generalized to other ethnicities. Such considerations are crucial in the planning of orthodontic planning to craft the facial esthetics of the individual patient. For example, African American patients are more often treatment planned for extractions as their profiles are more convex and better able to withstand a decrease in convexity caused by removal of teeth.

Another important trait that has been investigated is tooth size. It is crucial in understanding the basis for orthodontic crowding and Bolton discrepancies. There are a variety of studies that have examined the relationship between tooth size and ethnicity. Certain studies have reported that those of African descent have larger teeth than individuals of Caucasian descent (Lavelle, 1972; Merz, 1991). Other studies have found that Hispanic population had significant tooth size differences when compared to Caucasian populations but similar tooth size differences to African-American populations (Smith, 2000). In regards to Bolton ratios, one study found a statistically significant difference in prevalence of anterior tooth size discrepancies with African American subjects showing a higher prevalence than Caucasian or Hispanic study participants (Johe, 2000).

2.4 Review of ABO Blood Group Classification System

As previously mentioned, another individual patient characteristic that has been studied in dentistry and medicine albeit, never in orthodontics, is blood type. The ABO blood group classification system consists of identifying antigens, which are present on erythrocytes, as well as, a variety of other cell types in each individual (Pendu, 2021). These antigens are carbohydrates of which their synthesis first requires the production of histo-blood group H pre-cursor antigens (Pendu, 2021). Once the precursor antigen is catalyzed, either α1,3 linkage of N-acetylgalactosamine or galactose antigen is attached to the unit, and this generates the A (former) or B (latter) antigens (Pendu, 2021). The A and B enzymes are catalyzed by specific alleles linked to the ABO gene, while the O allele means that no active enzymes have been generated (Pendu, 2021). This is how blood types A, AB, B, and O are defined. It is also important to note that each ABO blood type has anti-antibodies. For example, the O blood type has anti-antibodies against A and B. Those with blood type B have anti-antibodies against A and those with blood type A have anti-antibodies against B. Those with blood type AB have no anti-antibodies (Pendu, 2021).

Importantly, blood groups have been associated with susceptibility to a variety of viral diseases such as noroviruses and rotaviruses (Pendu, 2021; Van Alsten, 2021). These viruses act by attaching to the carbohydrate antigens in the intestinal mucosa and they have mutated into specific strains that specialize on infecting and attaching to those with different blood types (Pendu, 2021). Furthermore, ABO blood groups are known to

have an effect on susceptibility to thrombosis including myocardial infarction, atherosclerosis, venous thromboembolism, and cardiovascular ischemic events (Pendu, 2021). One explanation for this lies in von Willebrand factor, which is known to be higher in those with non-O blood types. The reason for this is that von Willebrand factor expresses the antigens linked to each person's ABO phenotype (Pendu, 2021). It's clearance is slowed down in the presence of A or B antigens, and this results in higher plasma levels in those with A blood type, B blood type, or AB blood type (Pendu, 2021).

2.5 Blood groups and Inflammation

Blood type has also been linked to an individual person's inflammatory response. Some genome-wide studies have found associations between ABO locus and levels of circulating inflammatory markers, such as TNF-alpha, with individuals of blood group O having higher levels of TNF-alpha (Melzer, 2008). Other studies have found associations between different inflammatory markers and blood type with blood type B being associated with soluble vascular cell adhesion molecule-1 and blood type A being associated with soluble E-selectin and intercellular adhesion molecule-1 (Sliz, 2019). Another study by Van Alsten, found ten different inflammatory markers that were mediated by blood type. Of those, three were associated with ABO blood types (Van Alsten, 2021). Two of these were receptors for molecules in the VEGF superfamily. These receptors inhibit outgrowth of blood and lymphatic vessels (Van Alsten, 2021). Individuals with blood type A had lower levels of sVEGFR2 and sVEGFR3. Interestingly, lower levels of these markers are associated with lung, pancreatic, ovarian, and gastrointestinal cancers (Van Alsten, 2021).

The third marker found associated with ABO blood groups by Van Alsten was sGP130. This important marker inhibits the IL-6 signaling cascade. IL-6 functions to recruit T-cells to areas of inflammation and elevated levels of sGP130 have been linked to high blood pressure and increased risk of cardiovascular events in humans (Van Alsten, 2021). In this study, individuals with type A blood were found to have lower levels of sGP130 than individuals of type O or B blood (Van Alsten, 2021). These gene-mediated inflammatory factors are complex and understanding is still incomplete, but what is certain is that individuals with different blood types respond differently to inflammatory processes and have different susceptibilities to a variety of diseases. Since inflammation is an integral part of orthodontic tooth movement, it is very probable that blood type affects orthodontics treatment.

2.6 Review of COVID-19 Virus and Inflammatory Effects

Another disease that has important and unpredictable inflammatory processes is COVID-19. COVID-19 is an enveloped, positive strand RNA molecule (Mathew, 2021). The envelope consists of three main components: the envelope protein, the spike protein, and the membrane protein (Mathew, 2021). The spike protein functions in viral entry while the membrane and envelope proteins function in viral assembly (Mathew, 2021). Figure 1 depicts an image of the structure of coronavirus (Mathew, 2021).

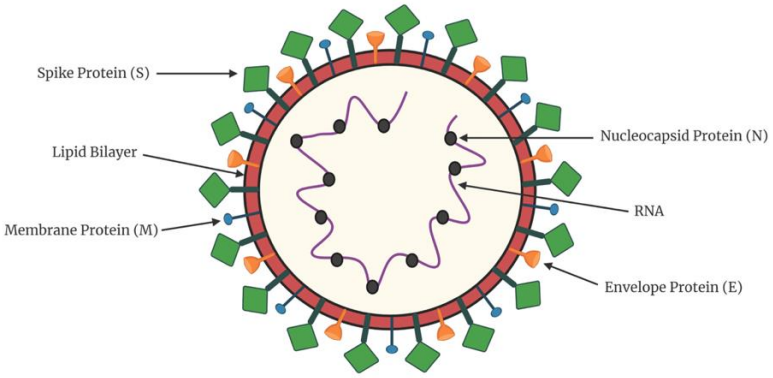

Figure 1: Structure of a Coronavirus (Mathew, 2021)

Most individuals who are infected with COVID-19 will exhibit mild or moderate illness, but some individuals are at higher risk of developing severe disease and becoming hospitalized (Mathew, 2021). The elderly, or immunocompromised (transplant, diabetes, or cancer patients) are thought to be at higher risk, along with those who have cardiovascular diseases (Sheikhi, 2020). However, sometimes, young adults with no pre-existing conditions exhibit severe disease for reasons unbeknownst to doctors and specialists. Common symptoms of COVID-19 include dry cough, fatigue, fever, muscle pain, headache, nausea, sore throat, loss of taste and smell (Mathew, 2021). As previously mentioned, when the COVID-19 virus enters the cell, this is mediated by the spike protein. The spike protein has three sections: the ectodomain, a single transmembrane anchor, and an intracellular tail (Mathew, 2021). The ectodomain has two subunits- one of which attaches to the host cell surface receptor and the other which joins the membrane of the host cell and allows entry of viral particles into the now adulterated cell (Mathew, 2021). More specifically, SARS-CoV2 recognizes human host cells by binding to the receptor ACE2, CD147, and TMPRESS2 (Mathew, 2021). SARS-CoV2 mainly targets ciliated

bronchial epithelial cells and type 2 pneumocytes (Wong, 2021). However, unfortunately, the ACE2 receptor exists among a variety of cells in the human body, including cells in the kidney, liver, lung, heart, pancreas, endothelial regions, and of course the upper airway and lungs (Gheblawi, 2020).

The immune response to COVID-19 occurs in two stages. The first stage is the innate immune response which is also known as a first line of defense during any type of infection from a virus (Wong, 2021). During this stage, immune cells secrete interferons as well as cytokines. These begin the next stage of immune response, the adaptive immune response. It is thought that one of the key factors in severity of COVID-19 infection may lie in a person's innate immune response. For example, delayed production of type I interferons may lead to increased levels of inflammatory cells and a profuse immune response (Wong, 2021). During the adaptive immune response, CD8 T cells search for virus infected cells, while CD4 T cells prompt B cells to create COVID-19 antibodies. Some individuals have an immune response that is dysfunctional, and this can result in an increase in innate immune cells and reduction in lymphocytes, and a delayed type I interferon response (Wong, 2021). In other words, the adaptive immune phase is retarded. This can result in more serious disease because the virus is allowed to replicate unchecked causing the viral load to be higher than normal (Wong, 2021).

The inflammatory effects of COVID-19 are still being studied. Some patients exhibit a massive immune system response, and these same patients are often the ones who develop more serious forms of the disease (Wong, 2021). This immune response can involve a variety of inflammatory markers or abnormal immune cells (Wong, 2021). For

example, some studies on deceased COVID-19 patients have shown upregulated expression of VEGF-A and VEGF-C (Ackermann, 2020). Many physicians refer to this as a cytokine storm (Wong, 2021). In short, the reactive effects of an overactive immune system is more damaging to the body than the virus itself. Cytokines are small proteins released by immune cells that serve to manage and adjust the immune system. A few examples include chemokines, interleukins and TNF, among others (Wong, 2021). If there is excessive cytokine release, this creates a storm. Cytokine storms can result in acute respiratory distress syndrome as well as hyperinflammation of the lungs (Wong, 2021). Autopsies and studies of deceased individuals with COVID-19 have yielded evidence that these patients may have undergone cytokine storms showing increased amounts of lymphocytes, macrophages, monocytes with reduced levels of CD4+, CD8+ T cells, and natural killer cells (Wong, 2021). Other inflammatory markers such as procalcitonin, C-reactive protein, serum ferritin, IL-2R, IL-6, IL-8, TNF-alpha are found to be elevated in those with severe COVID (Wong). This mechanism is the source of multi-organ damage in patients with severe COVID-19 (Wong, 2021). The unrestrained release of cytokines can result in vascular injury as well (Wong, 2021).

Such demographic trends should be considered in orthodontic treatment planning. Clearly, there are factors linked to each individual patient that affect treatment planning and treatment time. These differences merit further investigation to elucidate whether these factors ought to be counted in the diagnostic, planning of treatment, and mechanical execution stages of orthodontic treatment.

CHAPTER 3

AIMS OF THE INVESTIGATION

This project was conducted to fulfill the requirements for a MS in Oral Health Sciences from Temple University Graduate School. The aim of this study is to conduct a systematic review and meta-analysis to investigate whether patients' ABO blood types affect likelihood of COVID-19 infection and severity. Another aim is to relate these findings to tooth movement.

CHAPTER 4

MATERIALS AND METHODS

4.1 Data Sources and Search Strategy

The following databases were searched: Pubmed, DOSS, Mbase, Cochrane, Web of Science. The following MeSH terms were used: "ABO Blood-Group System/administration and dosage"[Mesh] OR "ABO Blood-Group System/adverse effects"[Mesh] OR "ABO Blood-Group System/anatomy and histology"[Mesh] OR "ABO Blood-Group System/blood"[Mesh] OR "ABO Blood-Group System/drug effects"[Mesh] OR "ABO Blood-Group System/genetics"[Mesh] OR "ABO Blood-Group System/immunology"[Mesh] OR "ABO Blood-Group System/metabolism"[Mesh] OR "ABO Blood-Group System/pharmacology"[Mesh] OR "ABO Blood-Group System/therapeutic use"[Mesh] We limited the search to studies published in or translated to English and published after the year 2000. To ensure a comprehensive search, research references were manually screened to identify additional qualified studies. Through this method, 26 additional studies were found and after reading the studies, two were excluded.

4.2 Inclusion and Exclusion Criteria

Studies involving ABO blood type and COVID-19 infection or outcomes were included. Studies conducted amongst subjects of all ages are included. Any study that used a blood group classification other than ABO was excluded. Correspondences, reports, and letters to the editor were included if they contained original data. Opinion pieces, animal studies and in vitro studies and studies conducted before the year 2000 were excluded. Studies not available in English or with lack of proper data analysis were excluded, as were studies not relevant to the subject.

4.3 Study selection

Studies were independently assessed by two reviewers (MM and ARL). The two reviewers determined if the studies fit into the eligibility criteria by reading the title and abstract. Any conflicts were resolved by a meeting and discussion of the two reviewers.

4.4 Data Extraction and Quality Assessment

One reviewer extracted the data from the included studies using a template which contained the following information: first author, year, country, characteristics of participants (age, gender, case and control selection), characteristics of the study (study design, sample size), outcomes, findings, appraisal score, and relative risk/odds ratio/effect

size. The Joanna Briggs Institute (JBI) critical appraisal tool was used to evaluate the methodological quality of the eligible studies. The JBI is an evidence based organization which was formed to create and standardize methodology for conducting systematic reviews. Pilot tests of this tool found that it had high validity, acceptability, and was easy and timely to complete (Munn, 2014). The JBI appraisals which were used are included in Appendix A. Quality assessments were performed by two researchers (ARL and MM) and if any discrepancies arose, they were resolved through discussion between the two authors. For the case control study appraisal, greater importance was given to questions 1, 2, 4, and 5. For the cohort study appraisal, greater importance was given to questions 1, 2, and 3. All questions for the systematic review and meta-analysis appraisal were weighed equally.

4.5 Statistical Analysis

Studies which included odds ratio in their statistical analysis and COVID-19 infection as an outcome were included in the meta-analysis. Overall, 15 studies met this criteria, however, two of the studies did not have adequate data and were excluded from the Forest Plots. Statistical analysis for the studies included in the meta-analysis were performed using SPSS version 28 using the meta-analysis function for binary outcomes using log odds ratio. Effect size and 95% confidence interval (CIs) were calculated using a random effects model to measure the association between ABO blood group and infection. Publication bias was evaluated using funnel plots. Forest plots were generated to indicate the pooled results. A value of $p<0.05$ was determined to be statistically significant.

CHAPTER 5

RESULTS

5.1 Literature Search

A thorough search yielded 2770 studies from the databases, of which, 0 were duplicates. The remaining 2770 records were filtered using the title and abstract, and 2734 were excluded because they included topics that were not relevant. The remaining studies underwent full text review and 15 were selected which met the criteria required to be included. Following a manual screening of each study's references, 26 additional reports were found and after reading the studies, two were excluded. Additionally, four narrative literature review articles were found which were not included in the data analysis but will be discussed qualitatively in the discussion. Overall, 39 studies were included in the systematic review and 13 of those studies were included in the meta-analysis. The detailed search process is demonstrated in Figure 2.

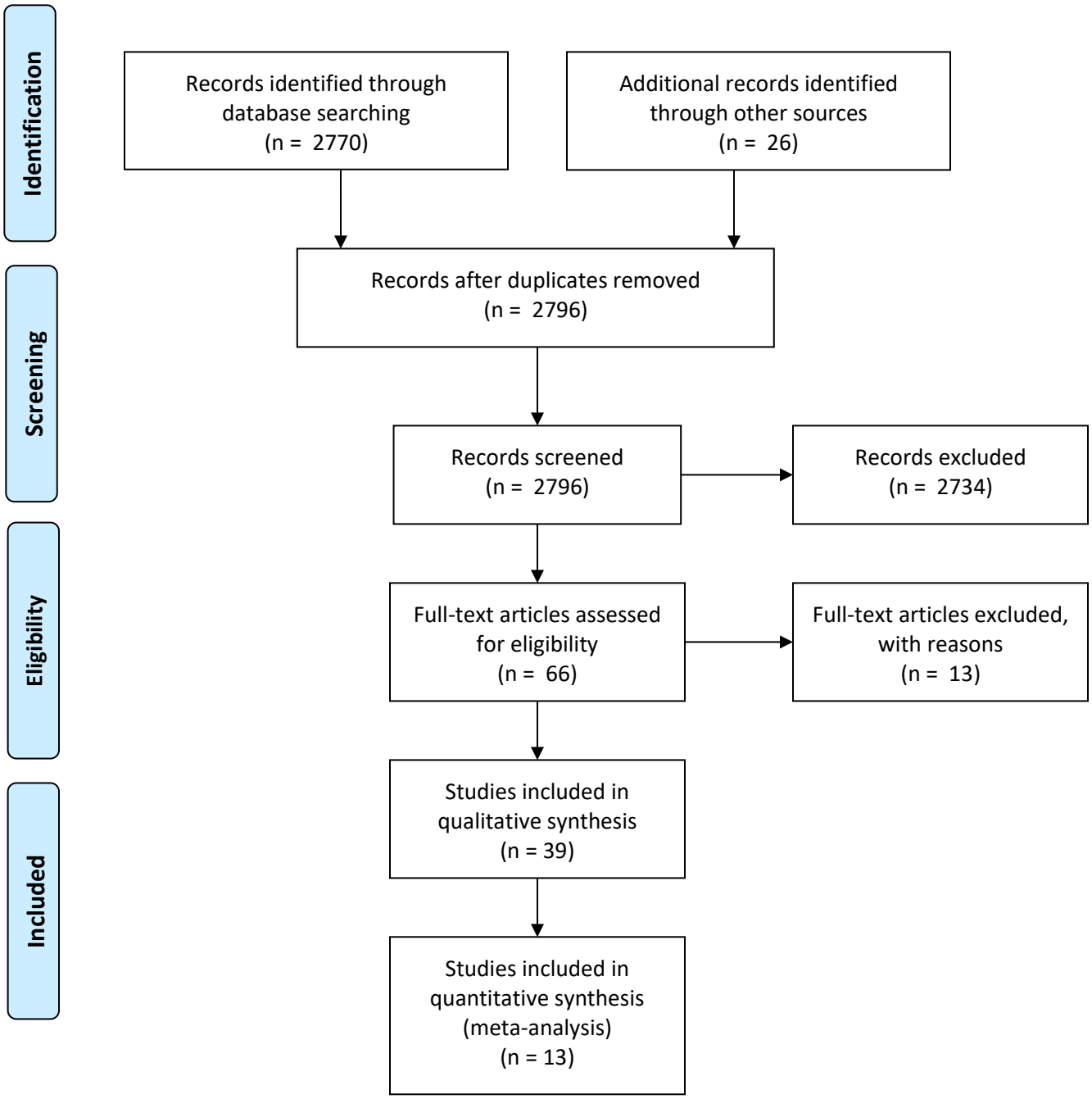

Figure 2: PRISMA Flow Diagram Showing Selection of Studies

5.2 Study Characteristics and Quality Assessment

29 of the studies were published in 2020, and ten were published in 2021. Selected characteristics of the study participants are shown in Table 1 (Appendix B). Sixteen of the studies were retrospective case control studies, two were prospective cohort studies, seventeen were retrospective cohort studies, and four were systematic reviews. Seven of the studies were conducted in China, one in Italy, one in Italy and Spain, two in Spain, one in Sweden, one in Bangladesh, two in Turkey, one in India, one in Saudi Arabia, one in Kuwait, four in Iran, one in Bahrain, one in Iraq, one in Australia, two in Canada, two in France, one in Denmark, two in the United Kingdom, two in Brazil, and five in the United States. Most of the studies included adult participants older than 18 years of age. Most of the COVID-19 diagnosis were confirmed via an RT-PCR COVID test. Many participants in the control group were healthy blood donors or data from studies of blood type prevalence on the general population, however, seven studies used control groups that tested negative for COVID-19. Of the qualified studies, JBI scores ranged from one to eleven points (highest possible score was ten for case control appraisals and cohort appraisals and eleven for meta-analysis/systematic review appraisals). Four studies were rated as very low quality, eighteen low quality, ten of moderate quality, and seven high quality.

5.3 Association Between Blood Group A and COVID-19 Infection

The 13 studies included in the meta-analysis using a random-effects model showed increased odds of COVID-19 infection for those with blood group A as compared to non-A blood group participants (ES= -0.174, 95% CI= -0.248 to -0.100, $p<0.001$) (Figure 3). In other words, there was an association between those who have blood group A and COVID-19 infection. Visual inspection of the funnel plot (Figure 4) indicated symmetry and did not yield any evidence of publication bias. In regards to COVID-19 severity, Mahmud et al. found no difference in symptoms between COVID patients with blood group A versus all other blood types but persistent positivity at 14 days was more frequent in those with blood group A (Mahmud, 2021). Al-Youha et al., found a higher odds of blood group A developing pneumonia as compared to other blood groups (Al-Youha, 2021). Hoiland et al., found a higher proportion of those with blood group A required mechanical ventilation, CRRT, and had prolonged ICU admission (Hoiland, 2020). Four studies (Kibler, 2020; Leaf Karp, 2020; Hulstrom, 2020; Sohlpour, 2020) found that blood type A may be a risk factor for critical illness. Zietz et al., found a decreased risk of intubation relative to blood type O (Zietz, 2020). Additionally, one study (Zalba-Marcos, 2020) found increased risk of other infections relative to other blood types. In regards to mortality, six studies (Ad'hiah, 2020; Kibler., 2020; Liu 2021., Zhao. 2021;, Hulstrom, 2020 and Muniz-Diaz, 2020) found an association of blood group A with COVID-19 related death. One study (Zietz, 2020) found a decreased risk of death of blood type A relative to blood type O.

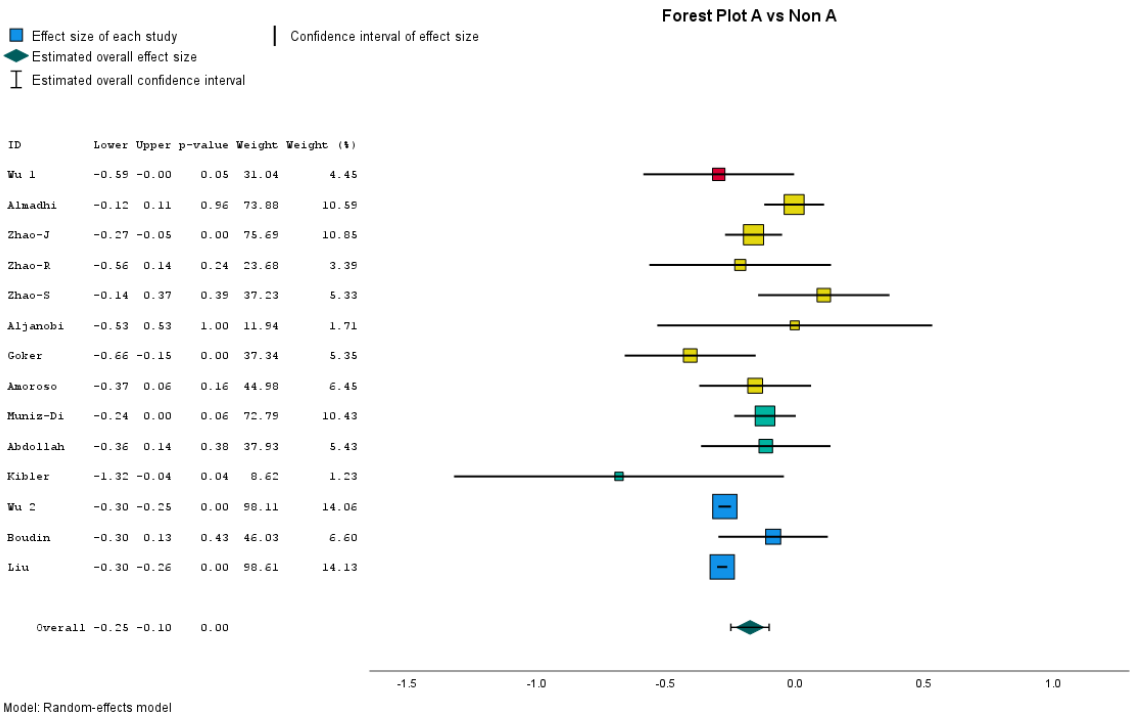

Figure 3: A vs Non-A

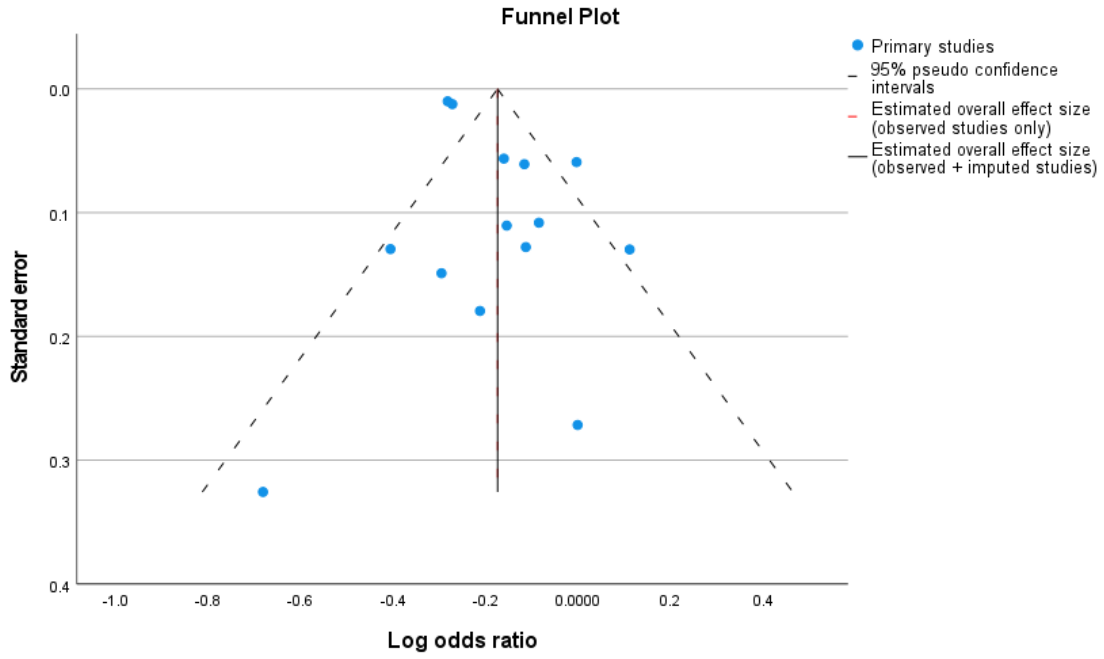

Figure 4: A vs Non-A Funnel Plot with 95% Pseudo Confidence Interval Limits

5.4 Association between Blood Group B and COVID-19 Infection

The 13 studies included in the meta-analysis using a random-effects model showed no increased odds of COVID-19 infection for those with blood group B as compared to non-B blood group participants (ES= -0.010, 95% CI= -0.107 to 0.086, p=0.831) (Figure 5). In other words, there was no association between having blood group B and COVID-19 infection. Visual inspection of the funnel plot (Figure 6) indicated symmetry and did not yield any evidence of publication bias. In regards to COVID-19 severity, one study found an increased risk of intubation (Zietz, 2020) and one study found increased risk of admission to ICU and thrombotic complications (Zalba-Marcos, 2020). As for mortality, one study found a decreased risk of death (Zietz, 2020).

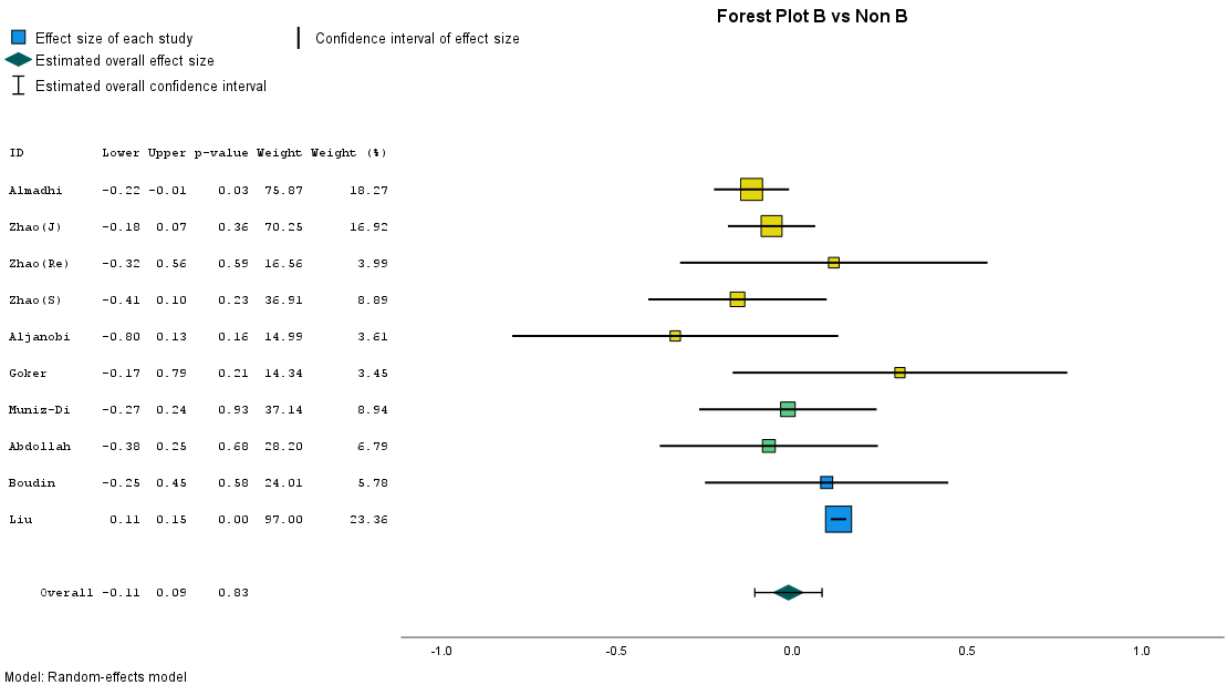

Figure 5: B vs Non-B

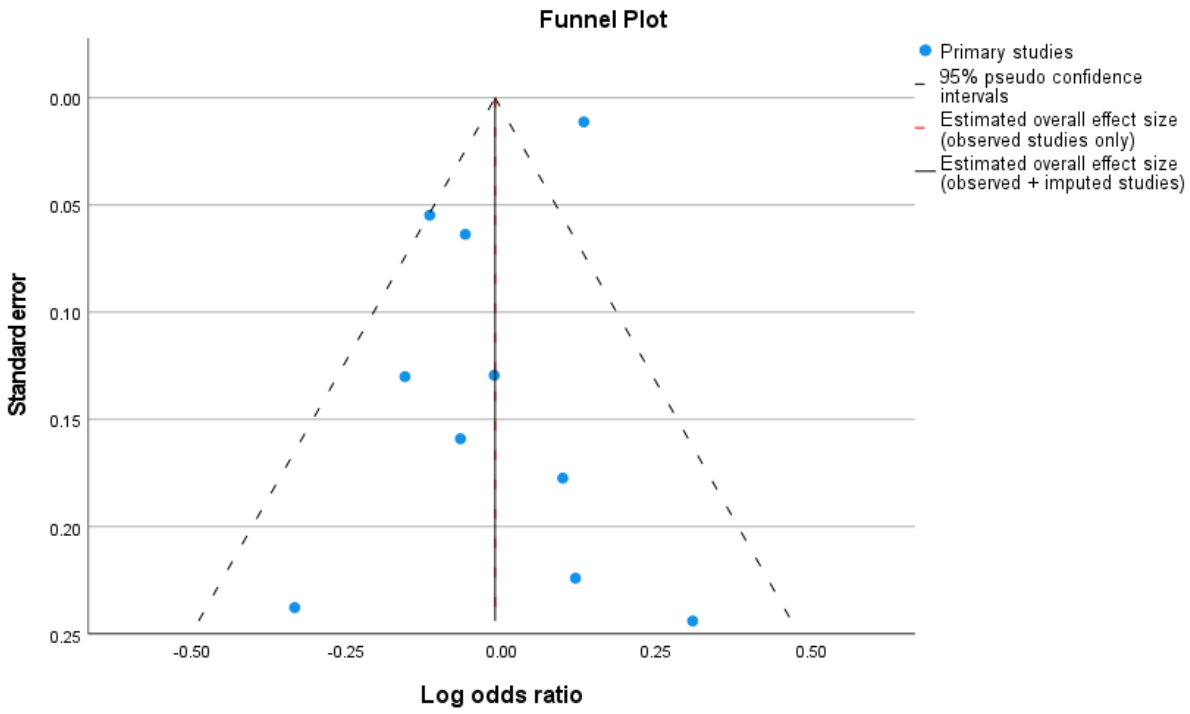

Figure 6: B vs Non-B Funnel Plot with 95% Pseudo Confidence Interval Limits

5.5 Association Between Blood Group AB and COVID-19 Infection

The 13 studies included in the meta-analysis using a random-effects model showed no increased odds of COVID-19 infection for those with blood group AB as compared to non-AB blood group participants (ES= -0.140, 95% CI= -0.344 to 0.064, p=0.179) (Figure 7). In other words, there was no association between having blood group AB and COVID-19 infection. Visual inspection of the funnel plot (Figure 8) indicated symmetry and did not yield any evidence of publication bias. Regarding COVID-19 severity, one study (Hoiland, 2020) found a higher proportion of those with blood group AB required mechanical ventilation, CRRT, and had prolonged ICU admission as compared to other

blood groups. Wu et al. reported an increased risk of severe COVID for those with blood type AB as did Hulstrom et al (Hulstrom, 2020). One study (Zietz, 2020) found an increased risk of intubation. Additionally, one study (Zalba-Marcos, 2020) found increased risk of infection relative to other blood types. Pertaining to mortality, three studies (Ad'hiah, 2020; Hulstrom, 2020; Zietz, 2020) noted an increased risk of dying of COVID-19 in individuals with this blood group.

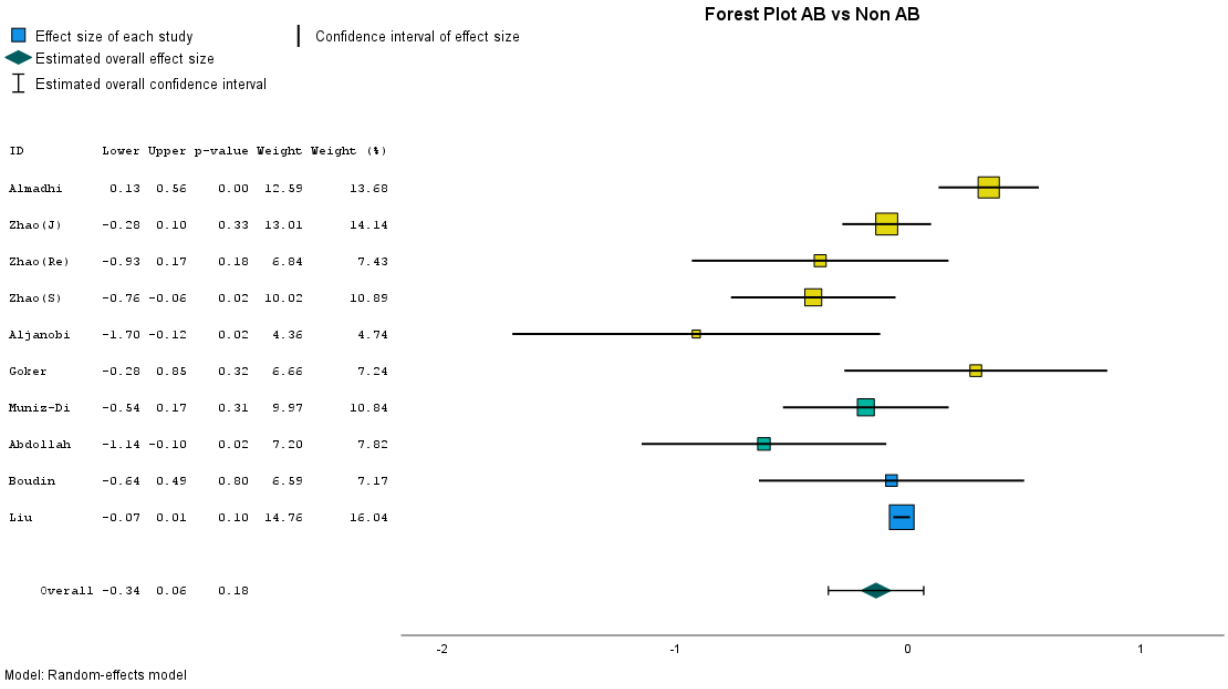

Figure 7: AB vs Non-AB

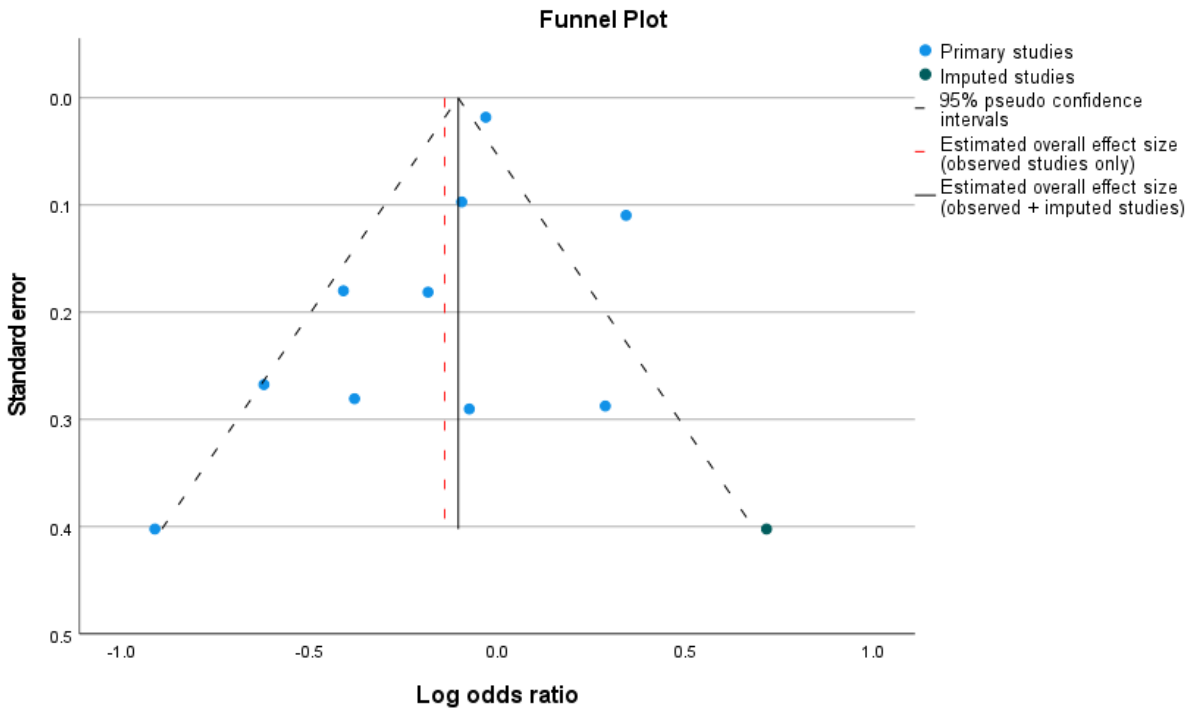

Figure 8: AB vs Non-AB Funnel Plot with 95% Pseudo Confidence Interval Limits

5.6 Association Between Blood Group O and COVID-19 Infection

The 13 studies included in the meta-analysis using a random-effects model showed decreased odds of COVID-19 infection as compared to non-O blood group participants (ES= 0.174, 95% CI= 0.086 to 0.261, p<0.001) (Figure 9). In other words, there was a protective association between for those who have blood group O, as related to COVID-19 infection. Visual inspection of the funnel plot (Figure 10) indicated symmetry and did not yield any evidence of publication bias. Also pertinent to COVID-19 severity, three studies (Leaf Karp, 2020; Zalba-Marcos, 2020 and Ray, 2020) detected that blood type O may be

a protective factor for critical illness. As for mortality, one study (Zhao, 2021.) found that type O blood was associated with decreased risk of death.

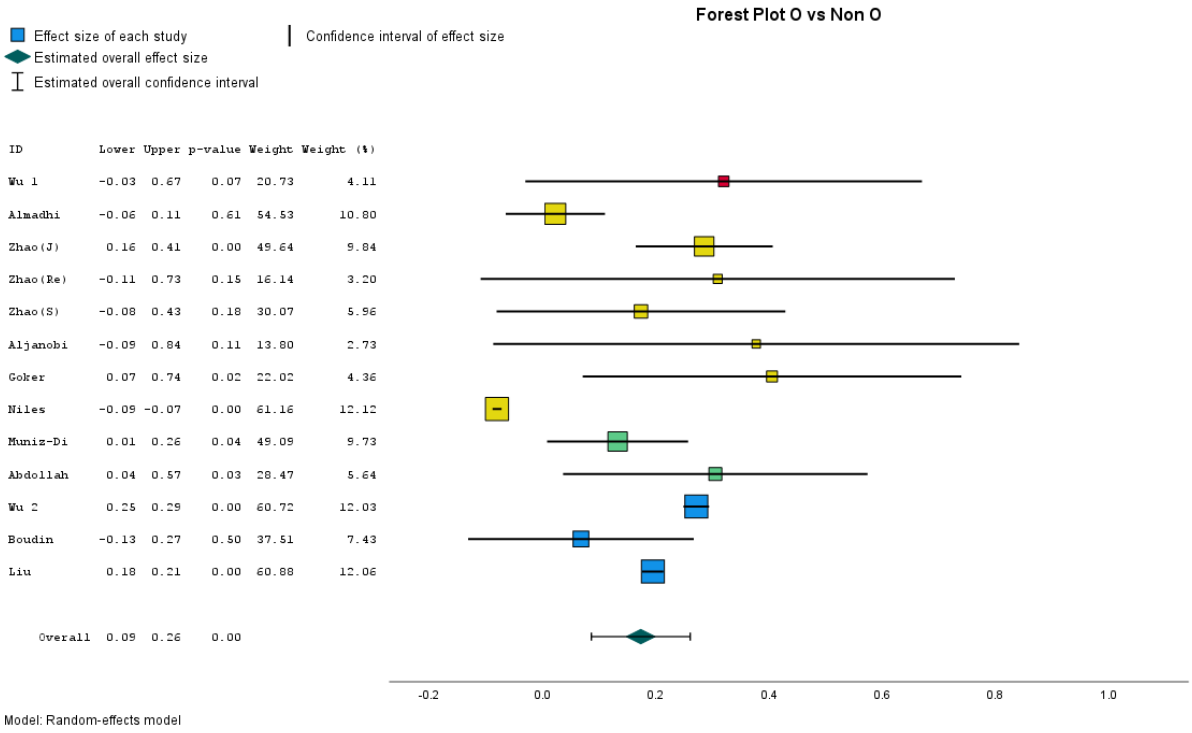

Figure 9: O vs Non-O

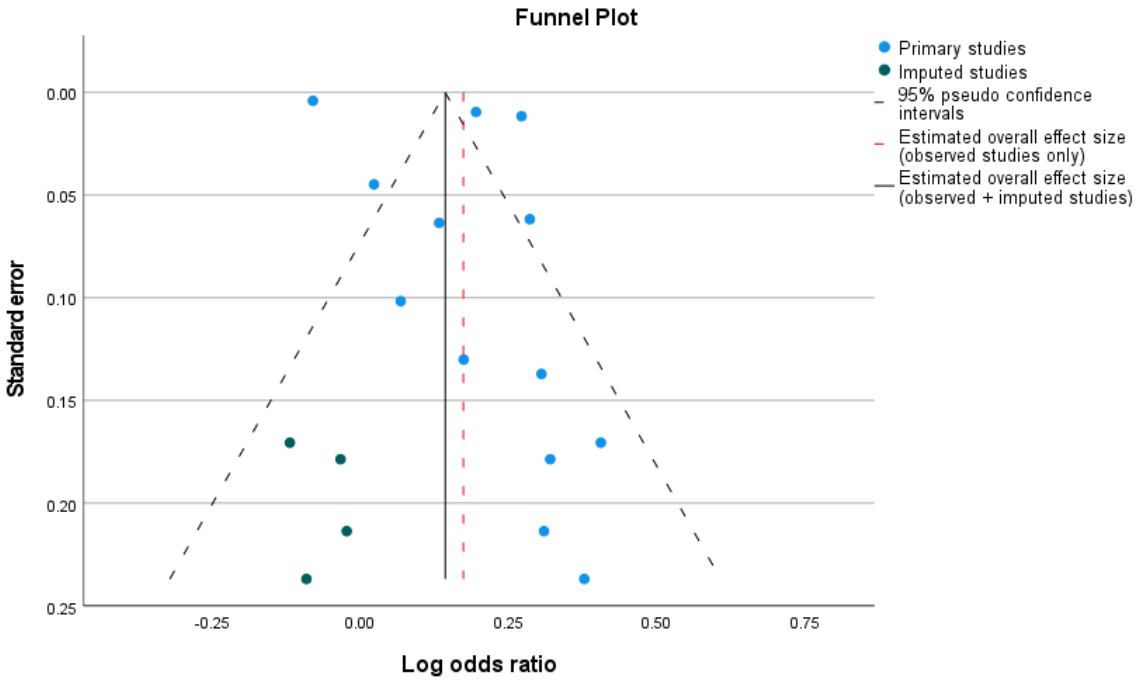

Figure 10: O vs Non-O Funnel Plot with 95% Pseudo Confidence Interval Limits

CHAPTER 6

DISCUSSION

We believe this study is one of the largest and most comprehensive systematic reviews and meta-analyses available in the current literature on COVID-19 infection and blood type. The meta-analysis presented consists of 13 studies while the systematic review consists of 39 studies. The meta-analysis data showed a statistically significant association of blood group A is with COVID-19 infection when compared to non for blood group-A. The data also showed a statistically significant protective association of blood group O, relative to COVID-19 infection when compared to non blood group O individuals. There was no statistically significant association of blood group B with COVID-19 infection, nor was there a statistically significant association of blood group AB. COVID-19 mortality and severity were not included in the meta-analysis, however, these outcomes were included in the systematic review. Unfortunately, studies yielded inconsistent results concerning these metrics; several studies finding increased risk of critical illness or death in those with blood type A, B, AB, and a protective effect of blood type O. However, one study found a protective effect of blood type A related to death. It is also important to note that nine studies found no difference in COVID-19 severity and six studies found no difference in mortality when comparing different ABO blood groups. Critical illness was a difficult metric to include in the meta-analysis, as each study had different definitions of what constituted critical COVID-19 illness, including but not limited to intubation, acute

kidney injury, pneumonia, mechanical ventilation, CRRT, prolonged ICU admission, and thrombotic complications.

6.1 Possible Mechanisms for Susceptibility of Blood Type to COVID-19 Infection

As for our findings related to COVID-19 infection, it was found that type A individuals are more susceptible to infection whereas, type O individuals are less susceptible. There are several mechanisms that may be responsible for this phenomenon. For example, there is some evidence that antibodies in the ABO system could block the S protein (on the COVID-19 virus) from interacting with angiotensin-converting enzyme 2 (Guillon, 2008). More specifically, Guillon et al. found that in Chinese hamster ovary cells, adhesion of S protein to ACE-2 was inhibited by anti-A antibodies (Guillon, 2008). Thus, these antibodies may play a protective role in blocking adhesion of COVID-19 virus and human receptor cells. This theory is in line with our findings of type O blood being protective, while type A holding increased risk. In contrast, it is inconsistent with our non-significant findings for individuals with type B blood and type AB blood. Had our study yielded results that type B blood is also protective and type AB blood is also at greater risk, this would truly be in line with Guillon et al's theory.

Another mechanism that has been discussed in the literature is the differential inhibition of infection between SARS-COV-2 viruses that exhibit different ABO phenotypes (Yamamoto, 2021; Miotto, 2021). This concept highlights the possibility that the antibodies created by each different blood type can react to antigens and block infection

between those with different ABO blood groups (Yamamoto, 2021). In simpler terms, COVID-19 viruses produced in those with B blood type will express B antigens that can infect group B or AB readily, with no antigen-antibody reactions. In contrast, group A COVID-19 viruses will have the ability to readily infect those with A or AB blood group (Yamamoto, 2021). This inhibition is by no means fully effective. Once infected, new COVID-19 viruses produced in the body exhibit the same ABO phenotype as their host with no issues reproducing. Hence, this phenomenon is only important for initial infection and not for progression of disease. Again, this theory nicely aligns with our findings of type O individuals being at lower risk of infection. Since type O individuals produce antibodies for both A and B, they would be at lower risk of infection from these individuals. This theory, however, does not align with our findings of type A blood being at the greatest risk of infection. According to this conjecture, individuals with type AB blood should be at highest risk of infection, as they produce neither A nor B antibodies, and would not have protection from individuals of any blood type.

A third theory that has been proposed is related to inflammatory markers, particularly IL-6 levels. Some studies have reported that individuals with type O blood have increased IL-6 levels (Dai, 2020). IL-6 functions as a proinflammatory cytokine which causes a cascade resulting in the synthesis of C-reactive protein (Bermudez, 2002). C-reactive protein is related to levels of ACE inhibitor which means that type O blood types have lower levels of ACE than other blood types (Dai, 2020). As the COVID-19 virus binds to the ACE receptor, this could provide an explanation for why type O blood

individuals seem to have a lower susceptibility to COVID-19 infection. This is consistent with the findings of our study.

6.2 Implications for Orthodontics

These findings have important potential implications for orthodontics and tooth movement. If one of the mechanisms for vulnerability to COVID-19 infection is levels of inflammation and orthodontics relies on inflammatory processes to move teeth, further exploration of this topic is crucial for clinicians. IL-6 is an important pro-inflammatory cytokine in orthodontics especially, in orthodontically induced inflammatory root resorption and it is known that IL-6 plays a role in triggering osteoclast formation and activation (Kunii, 2013). Some studies have shown that patients with severe inflammatory root resorption post-orthodontics, have elevated levels of IL-6 in their gingival crevicular fluid (Kunii, 2013) as compared to those who do not have severe root resorption after treatment. If those with type O blood have lower levels of IL-6, they may be less susceptible to root resorption when undergoing orthodontic treatment, while other blood types may be at higher risk. This could mean that precautionary measures should be taken for those with non-type O blood such as: slower orthodontic tooth movement, non-extraction treatment, or considering Invisalign® as a modality, rather than conventional metal braces. One caveat, however, is that it is still unknown whether IL-6 is a biomarker for orthodontically induced inflammatory root resorption or if it truly facilitates root resorption.

Furthermore, there is evidence that ACE-inhibitors, such as the medication Losartan, slow down orthodontic tooth movement (Makrygiannakis, 2018). Some animal

studies have shown that over-activation of the renin-angiotensin system can increase osteoclast activity and induce osteoporosis (Makrygiannakis, 2018). On the contrary, for patients on ACE-inhibitors, there is often an increase in bone density (Makrygiannakis, 2018). Studies observing orthodontic tooth movement in patients taking ACE-inhibitors have observed that levels of osteoclastic activity seem to be decreased, while osteoblastic activity increased (Makrygiannakis, 2018). If those with type O blood have antibodies that more readily block binding to the ACE-2 receptor, this could mean that levels of osteoclastic activity are naturally lower than in patients with types A, B or AB. As a result, osteoclastic activity may be lower and tooth movement might be slower, resulting in increased treatment time for these patients.

6.3 Strengths and Limitations

A major strength of this study is that it is one of the most comprehensive meta-analysis and systematic reviews available on COVID-19 infection and outcomes in the literature. Another important strength is that there was a low level of publication bias, as indicated by the Funnel plots. This is highly likely because there is a need for knowledge about the new COVID-19 virus, and studies were published regardless of whether or not they had significant findings. Even if a study did not yield a significant result, this was still meaningful and yielded important information on a topic that researchers were hungry to learn more about.

Despite its significant results, this study has several limitations. One main limitations is that there is a limited number of studies available on this topic. It is to be expected, as COVID-19 is a novel virus that has only been in existence since 2019. We also chose to limit the studies to English only, which further limited our sample. Another limitation is that many of the studies included in the systematic review had variability in specific outcomes and statistical analyses used. Accordingly, we specifically chose to focus on COVID-19 infection for the meta-analysis and not all 39 studies were included in the meta-analysis portion of this paper. Finally, it is important to note that most of the studies included were considered low or moderate quality; there were only three studies in the meta-analysis that were considered high quality.

6.4 Future Directions

This study is a high quality, thorough meta-analysis and systematic review on COVID-19 infection and blood types. The scientific community would benefit from additional methodologically strong studies on this topic regarding COVID and blood type. The next step in orthodontics could be a clinical study that incorporates routine blood drawing from orthodontic patients to determine their blood type. Such samples could enable observation of inflammatory markers and their activity throughout course of treatment. They can be monitored and tracked for applications of different metrics, such as root resorption, treatment time, and ankylosis.

Our study and findings were thorough, but COVID-19 is still a sizeable mystery. As the exploration of the mechanisms of SARS-CoV-2 continues, it may help elucidate how individual patient characteristics may feed into individual responses and treatment outcomes. Inquiries are still inquiry needed. Many questions need answers including, but not limited to post-COVID syndrome. How might it affect the treatment? Orthodontic specialists would do well to keep up-to-date with such research, and monitor the relevance and impact in tooth movement. Orthodontics patients deserve clinicians who are willing and eager to treat them as individuals. One way to deliver the best treatment based on diagnosis is to include exploration of blood type and other individual characteristics of the patient.

CHAPTER 7

CONCLUSIONS

The conclusions of this study are as follows:

- Results of our meta-analysis suggest that individuals with blood type A appear to have a greater susceptibility to COVID-19 infection
- Our findings also suggest that those with blood type O appear to have less susceptibility to COVID-19 infection
- Exploring individual patient characteristics such as blood type and elucidating the mechanism through which this may confer greater protection or vulnerability to COVID-19 is an important pathway to personalized medicine in other disciplines, such as orthodontics.

BIBIOLOGRAPHY

Abdollahi, A., Mahmoudi-Aliabadi, M., Mehrtash, V., Jafarzadeh, B., & Salehi, M. (2020). The Novel Coronavirus SARS-CoV-2 Vulnerability Association with ABO/Rh Blood Types. Iranian journal of pathology, 15(3), 156–160. https://doi.org/10.30699/ijp.2020.125135.2367

Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, et al. (2020). Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in covid-19. New England Journal of Medicine, 383:120–8.

Ad'hiah, A. H., Allami, R. H., Mohsin, R. H., Abdullah, M. H., AL-Sa'ady, A., & Alsudani, M. Y. (2020). Evaluating of the association between ABO blood groups and coronavirus disease 2019 (COVID-19) in Iraqi patients. The Egyptian Journal of Medical Human Genetics, 21(1), 50. https://doi.org/10.1186/s43042-020-00097

Ahmed I, Quinn L, Tan BK. (2021). COVID-19 and the ABO blood group in pregnancy: A tale of two multiethnic cities. International Journal of Laboratory Hematology. e45-e47. doi: 10.1111/ijlh.13355. PMID: 32996710; PMCID: PMC7537203.

Alcalde RE., et al. (2000). "Soft tissue cephalometric norms in Japanese adults". American Journal of Orthodontics and Dentofacial Orthopedics 118: 84-89.

Aljanobi, G. , Alhajjaj, A. , Alkhabbaz, F. and Al-Jishi, J. (2020) The Relationship between ABO Blood Group Type and the COVID-19 Susceptibility in Qatif Central Hospital, Eastern Province, Saudi Arabia: A Retrospective Cohort Study. Open Journal of Internal Medicine, 10, 232-238. doi: 10.4236/ojim.2020.102024.

Almadhi MA, Abdulrahman A, Alawadhi A, Rabaan AA, Atkin S, AlQahtani M. The effect of ABO blood group and antibody class on the risk of COVID-19 infection and severity of clinical outcomes. (2021). Scientific Reports. 11(1):5745. doi: 10.1038/s41598-021-84810-9. PMID: 33707451; PMCID: PMC7952683.

Al-Youha SA, Alduaij W, Al-Serri A, Almazeedi SM, Al-Haddad M, Jamal MH, Shih AW, Al-Sabah SK. (2021). The impact of ABO blood groups on clinical outcomes and susceptibility to COVID-19: A retrospective study in an unselected population. Transfusion. 61(5):1631-1641. doi: 10.1111/trf.16365. PMID: 33682150; PMCID: PMC8250670.

Amoroso A, Magistroni P, Vespasiano F, Bella A, Bellino S, Puoti F, Alizzi S, Vaisitti T, Boros S, Grossi PA, Trapani S, Lombardini L, Pezzotti P, Deaglio S, Brusaferro S, Cardillo M. (2021). Italian Network of Regional Transplant Coordinating Centers. HLA and AB0 Polymorphisms May Influence SARS-CoV-2 Infection and COVID-19 Severity. Transplantation. 105(1):193-200. doi: 10.1097/TP.0000000000003507. PMID: 33141807.

Barnkob MB, Pottegård A, Støvring H, Haunstrup TM, Homburg K, Larsen R, Hansen MB, Titlestad K, Aagaard B, Møller BK, Barington T. (2020). Reduced prevalence of SARS-CoV-2 infection in ABO blood group O. Blood Advances. 4(20):4990-4993. doi: 10.1182/bloodadvances.2020002657. PMID: 33057631; PMCID: PMC7594382.

Bermudez EA, Rifai N, Buring J, Manson JE, Ridker PM. Interrelationships among circulating interleukin-6, C-reactive protein, and traditional cardiovascular risk

factors in women. Arterioscler Thromb Vasc Biol. 2002 Oct 1;22(10):1668-73. doi: 10.1161/01.atv.0000029781.31325.66. PMID: 12377747.

Bhandari, P., Durrance, R. J., Bhuti, P., & Salama, C. (2020). Analysis of ABO and Rh Blood Type Association With Acute COVID-19 Infection in Hospitalized Patients: A Superficial Association Among a Multitude of Established Confounders. Journal of clinical medicine research, 12(12), 809–815. https://doi.org/10.14740/jocmr4382

Boudin L, Dutasta F, Relationship Between ABO Blood Groups and Coronavirus Disease 2019: Study Design Matters, Clinical Infectious Diseases, Volume 72, Issue 11, 1 June 2021, Page e918, https://doi.org/10.1093/cid/ciaa1473

Brezniak, N., & Ben-Ya'ir, S. (1989). Patient burnout—Behaviour of young adults undergoing orthodontic treatment. Stress Medicine, 5(3), 183-187. doi:10.1002/smi.2460050308

Cancer Genome Research and Precision Medicine. National Cancer Institute. (2017, May 3). Retrieved December 26, 2020, from https://www.cancer.gov/about-nci/organization/ccg/cancer-genomics-overview

Cavalli-Sforza, L. The Human Genome Diversity Project: past, present and future. Nat Rev Genet 6, 333–340 (2005). https://doi.org/10.1038/nrg1596

Chegni H, Pakravan N, Saadati M, Ghaffari AD, Shirzad H, Hassan ZM. Is There a Link between COVID-19 Mortality with Genus, Age, ABO Blood Group Type, and ACE2 Gene Polymorphism? Iran J Public Health. 2020 Aug;49(8):1582-1584. doi: 10.18502/ijph.v49i8.3910. PMID: 33083341; PMCID: PMC7554399.

Conradie, M., Conradie, M.M., Kidd, M. et al. Bone density in black and white South African women: contribution of ethnicity, body weight and lifestyle. Arch Osteoporos 9, 193 (2014). https://doi.org/10.1007/s11657-014-0193-0.

Cooke MS., et al. “Cephalometric ‘‘standards’’ for the southern Chinese”. European Journal of Orthodontics 10 (1988): 264- 272.

Dai X. ABO blood group predisposes to COVID-19 severity and cardiovascular diseases. European Journal of Preventive Cardiology. 2020;27(13):1436-1437. doi:10.1177/2047487320922370

Darendeliler, M. A., & Joho, J. (1993). Magnetic activator device II (MAD II) for correction of Class II, division 1 malocclusions. American Journal of Orthodontics and Dentofacial Orthopedics, 103(3), 223-239. doi:10.1016/0889-5406(93)700037

Davidovitch, Z., Korostoff, E., Finkelson, M. D., Yost, R. W., Montgomery, P. C., Steigman, S., & Shanfeld, J. L. (1980). Effect of electric currents on gingival cyclic nucleotides in vivo. Journal of Periodontal Research, 15(4), 353-362. doi:10.1111/j.1600-0765.1980.tb00292.x

Davidovitch, Z., Finkelson, M. D., Steigman, S., Shanfeld, J. L., Montgomery, P. C., & Korostoff, E. (1980). Electric currents, bone remodeling, and orthodontic tooth movement. American Journal of Orthodontics, 77(1), 33-47. doi:10.1016/0002-9416(80)90222-5.

de Freitas Dutra V, Bonet-Bub C, Yokoyama APH, Achkar R, Machado RRG, Assunção M, Candelária G, Soares CP, Fachini RM, Fontão-Wendel R, Hamerschlak N, Reis LFL, Araujo DB, Nudelman V, Pinho JRR, Rizzo LV, Sakashita AM, Scuracchio

P, Durigon EL, Wendel S, Kutner JM. Anti-A and SARS-CoV-2: an intriguing association. Vox Sang. 2021 May;116(5):557-563. doi: 10.1111/vox.13044. Epub 2021 Mar 2. PMID: 33650690; PMCID: PMC8013368.

Dzik S, Eliason K, Morris EB, Kaufman RM, North CM. COVID-19 and ABO blood groups. Transfusion. 2020 Aug;60(8):1883-1884. doi: 10.1111/trf.15946. Epub 2020 Aug 1. PMID: 32562280; PMCID: PMC7323215.

Edgren, G., et al. “Risk of Gastric Cancer and Peptic Ulcers in Relation to ABO Blood Type: A Cohort Study.” American Journal of Epidemiology, vol. 172, no. 11, ser. 1, 11 Dec. 2010, pp. 1280–1285. 1, doi:10.1093/aje/kwq299.

Ellinghaus D, Degenhardt F, Bujanda L et al. Genomewide Association Study of Severe Covid-19 with Respiratory Failure. New England Journal of Medicine. 2020 Oct 15;383(16):1522-

1534. doi: 10.1056/NEJMoa2020283. Epub 2020 Jun 17. PMID: 32558485; PMCID: PMC7315890.

Evanko AM., et al. “Mesh diagram analysis: developing a norm for Puerto Rican Americans”. The Angle Orthodontist 67 (1997): 381-388.

Fan, Q., Zhang, W., Li, B., Li, D. J., Zhang, J., & Zhao, F. (2020). Association Between ABO Blood Group System and COVID-19 Susceptibility in Wuhan. Frontiers in cellular and infection microbiology, 10, 404.

https://doi.org/10.3389/fcimb.2020.00404

Feilden, Tom. “Most Scientists 'Can't Replicate Studies by Their Peers'.” BBC News, BBC, 22 Feb. 2017, www.bbc.com/news/science-environment-39054778.

Fernandes, C.L. (2004) Forensic ethnic identification of crania: the role of the maxillary sinus–a new approach. The American Journal of Forensic Medicine and Pathology 25: 302.

Figueroa, R., & Ferguson, D. J. (2005). Selective Alveolar Decortication for Rapid Surgical-Orthodontic Resolution of Skeletal Malocclusion. Journal of Oral and Maxillofacial Surgery, 63(8), 18-19. doi:10.1016/j.joms.2005.05.040

Frost, HM. (1983) "The Regional Acceleratory Phenomenon: A Review," Henry Ford Hospital Medical Journal : Vol. 31 : No. 1 , 3-9.

Gheblawi, M., Wang, K., Viveiros, A., Nguyen, Q., Zhong, J., Turner, A.J., Raizada, M.K., Grant, M.B., Oudit, G.Y., 2020. Angiotensin-converting enzyme 2: SARS-CoV-2 receptor and regulator of the renin-angiotensin system. Circ. Res. 126, 1457–1475. https://doi.org/10.1161/CIRCRESAHA.120.317015.

Gilliland, F D. “Ethnic Differences in Cancer Incidence: A Marker for Inherited Susceptibility?” Environmental Health Perspectives, vol. 105, no. suppl 4, 1 June 1997, pp. 897–900., doi:10.1289/ehp.97105s4897.

Göker H, Aladağ Karakulak E, Demiroğlu H, Ayaz Ceylan ÇM, Büyükaşik Y, Inkaya AÇ, Aksu S, Sayinalp N, Haznedaroğlu IC, Uzun Ö, Akova M, Özcebe OI, Ünal S. The effects of blood group types on the risk of COVID-19 infection and its clinical outcome. Turk J Med Sci. 2020 Jun 23;50(4):679-683. doi: 10.3906/sag-2005-395. PMID: 32496734; PMCID: PMC7379446.

Golinelli D, Boetto E, Maietti E, Fantini MP. The association between ABO blood group and SARS-CoV-2 infection: A meta-analysis. PLoS One. 2020 Sep 18;15(9):e0239508. doi: 10.1371/journal.pone.0239508. PMID: 32946531; PMCID: PMC7500631.

Graber, T.M., Vardimon, A.D., Magnetic force in orthodontics (1989), p. 35. 65th EOS Abstracts

Graber, T.M. Magnetic forces in orthodontics. Salzmann Memorial Lecture: AAO Annual Meeting, New Orleans (1988)

Graber, L. W., Vanarsdall, R. L., Vig, K. W., & Huang, G. J. (2017). Orthodontics: Current principles and techniques. St. Louis, MO: Elsevier.

Guillon P, Clément M, Sébille V, Rivain JG, Chou CF, Ruvoën-Clouet N, Le Pendu J. Inhibition of the interaction between the SARS-CoV spike protein and its cellular receptor by anti-histo-blood group antibodies. Glycobiology. 2008 Dec;18(12):1085-93. doi: 10.1093/glycob/cwn093. Epub 2008 Sep 25. PMID: 18818423; PMCID: PMC7108609.

He, Meian, et al. "ABO Blood Group and Risk of Coronary Heart Disease in Two Prospective Cohort Studies." Arteriosclerosis, Thrombosis, and Vascular Biology, U.S. National Library of Medicine, 14 Aug. 2012, www.ncbi.nlm.nih.gov/pmc/articles/PMC3488453/

Hoiland RL, Fergusson NA, Mitra AR, Griesdale DEG, Devine DV, Stukas S, Cooper J, Thiara S, Foster D, Chen LYC, Lee AYY, Conway EM, Wellington CL, Sekhon MS. The association of ABO blood group with indices of disease severity and

multiorgan dysfunction in COVID-19. Blood Adv. 2020 Oct 27;4(20):4981-4989. doi: 10.1182/bloodadvances.2020002623. PMID: 33057633; PMCID: PMC7594392.

Hoogeveen, E. J., Jansma, J., & Ren, Y. (2014). Surgically facilitated orthodontic treatment: A systematic review. American Journal of Orthodontics and Dentofacial Orthopedics, 145(4). doi:10.1016/j.ajodo.2013.11.019

Hultström, M., Persson, B., Eriksson, O. et al. Blood type A associates with critical COVID-19 and death in a Swedish cohort. Crit Care 24, 496 (2020). https://doi.org/10.1186/s13054-020-03223-8.

Hwang HS., et al. "Ethnic differences in the soft tissue profile of Korean and European-American adults with normal occlusion and well-balanced faces". The Angle Orthodontist 72 (2002): 72-80.

Ioi H., et al. "Comparison of cephalometric norms between Japanese and Caucasian adults in antero-posterior and verti- cal dimension". European Journal of Orthodontics 29 (2007): 493-499.

Jing, L, et al. "Ethnic Background and Genetic Variation in the Evaluation of Cancer Risk: A Systematic Review." PLoS ONE, vol. 9, no. 6, 2014, doi:10.1371/journal.pone.0097522.

Johe RS, Steinhart T, Sado N, Greenberg B, Jing S, Intermaxillary tooth-size discrepancies in different sexes, malocclusion groups, and ethnicities, American Journal of Orthodontics and Dentofacial Orthopedics, Volume 138, Issue 5, 2010, Pages 599-607.

Kaslick, Ralph S., et al. “Investigation of Periodontosis with Periodontitis: Literature Survey and Findings Based on ABO Blood Groups.” Journal of Periodontology, vol. 42, no. 7, 1 July 1971, pp. 420–427., doi:10.1902/jop.1971.42.7.420.

Kerem, Eitan, et al. “Highly Variable Incidence of Cystic Fibrosis and Different Mutation Distribution among Different Jewish Ethnic Groups in Israel.” Human Genetics, vol. 96, no. 2, 1 Sept. 1994, pp. 193–197., doi:10.1007/bf00207378.

Kibler, M., Dietrich, L., et al. (2020). Risk and Severity of COVID-19 and ABO Blood Group in Transcatheter Aortic Valve Patients. Journal of clinical medicine, 9(11), 3769. https://doi.org/10.3390/jcm9113769

Köle, H. (1959). Surgical operations on the alveolar ridge to correct occlusal abnormalities. Oral Surgery, Oral Medicine, Oral Pathology, 12(4), 413-420. doi:10.1016/0030-4220(59)90051-9

Kunii, R., Yamaguchi, M., Tanimoto, Y., Asano, M., Yamada, K., Goseki, T., & Kasai, K. (2013). Role of interleukin-6 in orthodontically induced inflammatory root resorption in humans. Korean journal of orthodontics, 43(6), 294–301. https://doi.org/10.4041/kjod.2013.43.6.294

Latz, C. A., DeCarlo, C., Boitano, L., Png, C., Patell, R., Conrad, M. F., Eagleton, M., & Dua, A. (2020). Blood type and outcomes in patients with COVID-19. Annals of hematology, 99(9), 2113–2118. https://doi.org/10.1007/s00277-020-04169-1.

Lavelle CLB, Maxillary and mandibular tooth size in different racial groups and in different occlusal categories, American Journal of Orthodontics, Volume 61, Issue 1, 1972, Pages 29-37.

Leaf, R. K., Al-Samkari, H., Brenner, S. K., Gupta, S., & Leaf, D. E. (2020). ABO phenotype and death in critically ill patients with COVID-19. British journal of haematology.

Lehrer, S., & Rheinstein, P. H. (2021). ABO blood groups, COVID-19 infection and mortality. Blood Cells, Molecules, and Diseases, 89, 102571.

Levi, J. E., Telles, P. R., Scrivani, H., Oliveira, F. P., Vieira, L. C., Dias, C. M., & Campana, G. (2020). Lack of association between ABO blood groups and susceptibility to SARS-CoV-2 infection. Hematology, Transfusion and Cell Therapy, 42, 541.

Lew, K.K., Foong, W.C. and Loh, E. (1993) Malocclussion prevalence in an ethnic Chinese population. Australian Dental Journal, 38, 442-449. doi:10.1111/j.1834-7819.1993.tb04759.x

Lew KK., et al. "Soft-tissue cephalometric norms in Chinese adults with esthetic facial profiles". Journal of Oral and Maxillofacial Surgery (1992): 1184-1189.

Li Y, Jacox LA, Little SH, Ko CC. Orthodontic tooth movement: The biology and clinical implications. Kaohsiung J Med Sci. 2018 Apr;34(4):207-214. doi: 10.1016/j.kjms.2018.01.007. Epub 2018 Feb 3. PMID: 29655409.

Li J, Wang X, Chen J. Association between ABO blood groups and risk of SARS-CoV-2 pneumonia. Br J Haematol. 2020;190:24–27.

Liu, Katherine A., and Natalie A. Dipietro Mager. "Women's Involvement in Clinical Trials: Historical Perspective and Future Implications." Pharmacy Practice, vol. 14, no. 1, 2016, pp. 708–708., doi:10.18549/pharmpract.2016.01.708.

Liu, N., Zhang, T., Ma, L., Zhang, H., Wang, H., Wei, W., et al. (2020). The Impact of ABO Blood Group on COVID-19 Infection Risk and Mortality: A Systematic Review and Meta-Analysis. Blood Rev. 48, 100785. doi: 10.1016/j.blre.2020.100785

Mahmud R, Rassel MA, Monayem FB, Sayeed SKJB, Islam MS, et al. (2021) Association of ABO blood groups with presentation and outcomes of confirmed SARS CoV-2 infection: A prospective study in the largest COVID-19 dedicated hospital in Bangladesh. PLOS ONE 16(4): e0249252. https://doi.org/10.1371/journal.pone.0249252

Makrygiannakis MA, Kaklamanos EG, Athanasiou AE, Does common prescription medication affect the rate of orthodontic tooth movement? A systematic review, European Journal of Orthodontics, Volume 40, Issue 6, December 2018, Pages 649–659, https://doi.org/10.1093/ejo/cjy001

Marron, M. "Insulin-Dependent Diabetes Mellitus (IDDM) Is Associated with CTLA4 Polymorphisms in Multiple Ethnic Groups." Human Molecular Genetics, vol. 6, no. 8, 1997, pp. 1275–1282., doi:10.1093/hmg/6.8.1275.

Mathew, A., Vignesh Balaji E, Pai, S., Kishore, A., Pai, V., & Chandrashekar, K. S. (2021). ABO phenotype and SARS-CoV-2 infection: Is there any correlation?. Infection, genetics and evolution : journal of molecular epidemiology and evolutionary genetics in infectious diseases, 90, 104751. https://doi.org/10.1016/j.meegid.2021.104751

Meikle, MC. The tissue, cellular, and molecular regulation of orthodontic tooth movement: 100 years after Carl Sandstedt, European Journal of Orthodontics, Volume 28, Issue 3, June 2006, Pages 221–240, https://doi.org/10.1093/ejo/cjl001

Melzer D, Perry JRB, Hernandez D, Corsi AM, Stevens K, et al. (2008) A Genome-Wide Association Study Identifies Protein Quantitative Trait Loci (pQTLs). PLOS Genetics 4(5): e1000072. https://doi.org/10.1371/journal.pgen.1000072

Merz ML, Isaacson RJ, Germane N, Rubenstein LK, Tooth diameters and arch perimeters in a black and a white population, American Journal of Orthodontics and Dentofacial Orthopedics, Volume 100, Issue 1, 1991, Pages 53-58.

Miotto M, Di Rienzo L, Gosti G, Milanetti E, Ruocco G (2021) Does blood type affect the COVID-19 infection pattern?. PLOS ONE 16(5): e0251535.https://doi.org/10.1371/journal.pone.0251535

Miyajima K., et al. "Craniofacial structure of Japanese and European-American adults with normal occlusions and well-balanced faces". American Journal of Orthodontics and Dentofacial Orthopedics (1996).

Mohammed, AO., et al. "Relationship of the Sickle Cell Gene to the Ethnic and Geographic Groups Populating the Sudan." Public Health Genomics, vol. 9, no. 2, Apr. 2006, pp. 113–120., doi:10.1159/000091489.

Muñiz-Diaz, E., Llopis, J., Parra, R., Roig, I., Ferrer, G., Grifols, J., et al. (2021). Relationship Between the ABO Blood Group and COVID-19 Susceptibility, Severity and Mortality in Two Cohorts of Patients. Blood Transfusion 19 (1), 54. doi: 10.2450/2020.0256-20

Munn, Z., Moola, S., Riitano, D., & Lisy, K. (2014). The development of a critical appraisal tool for use in systematic reviews addressing questions of prevalence. International journal of health policy and management, 3(3), 123–128. https://doi.org/10.15171/ijhpm.2014.71

Nikawa, Hiroki, et al. “Denture Stomatitis and ABO Blood Types.” The Journal of Prosthetic Dentistry, vol. 66, no. 3, Sept. 1991, pp. 391–394., doi:10.1016/0022-3913(91)90268-2.

Niles, J.K.; Karnes, H.E.; Dlott, J.S.; Kaufman, H.W. Association of ABO/Rh with SARS-CoV-2 positivity: The role of race and ethnicity in a female cohort. Am. J. Hematol. 2020, 96, E23–E26.

O’Brien, K. (2020). Short steps on how to read a paper. Part 2: filtering papers. Kevin O’Brien’s Orthodontic Blog.

Onyeaso, C.O. (2004) Prevalence of malocclusion among adolescents in Ibadan, Nigeria. American Journal of Orthodontics & Dentofacial Orthopedics, 126, 604-607. doi:10.1016/j.ajodo.2003.07.012

Park IC., et al. “A cephalometric study of Korean adults”. Ameri- can Journal of Orthodontics and Dentofacial Orthopedics 96 (1989): 54-59.

Pendu JL, Breiman A, Rocher J, Dion M, Ruvoën-Clouet N. ABO Blood Types and COVID-19: Spurious, Anecdotal, or Truly Important Relationships? A Reasoned Review of Available Data. Viruses. 2021 Jan 22;13(2):160. doi: 10.3390/v13020160. PMID: 33499228; PMCID: PMC7911989.

Pinto, A., Alves, L., Maltz, M., Susin, C., & Zenkner, J. (2018). Does the Duration of Fixed Orthodontic Treatment Affect Caries Activity among Adolescents and Young Adults? Caries Research, 52(6), 463-467. doi:10.1159/000488209

Pourali, F.; Afshari, M.; Alizadeh-Navaei, R.; Javidnia, J.; Moosazadeh, M.; Hessami, A. Relationship between blood group and risk of infection and death in COVID-19: A live meta-analysis. New Microbes New Infect. 2020, 37, 100743.

Proffit, W. R., Fields, H. W., Larson, B. E., & Sarver, D. M. (2019). Contemporary orthodontics. Philadelphia: Elsevier.

Quiñones, L, et al. "Ethnic Susceptibility to Lung Cancer: Differences in CYP2E1, CYP1A1 and GSTM1 Genetic Polymorphisms between French Caucasian and Chilean Populations." Cancer Letters, vol. 141, no. 1-2, July 1999, pp. 167–171., doi:10.1016/s0304-3835(99)00099-3.

Ray JG, Schull MJ, Vermeulen MJ. Association between ABO and Rh blood groups and SARS-CoV-2 infection or severe COVID-19 illness: a population-based cohort study. Ann Intern Med. 2021;174:308–315.

Ricketts RM, Divine Proportion in Facial Esthetics, Clinics in Plastic Surgery, Volume 9, Issue 4, 1982, Pages 401-422.

Rodan, G., Bourret, L., & Norton, L. (1978, February 10). DNA synthesis in cartilage cells is stimulated by oscillating electric fields. Retrieved January 10, 2021, from https://www.ncbi.nlm.nih.gov/pubmed/625660

Sandler, J. P. (1991). An attractive solution to unerupted teeth. American Journal of Orthodontics and Dentofacial Orthopedics, 100(6), 489-493. doi:10.1016/0889-5406(91)70089-f

Sheikhi, K., Shirzadfar, H., Sheikhi, M., 2020. A Review on Novel Coronavirus (Covid-19): Symptoms,Transmission and Diagnosis Tests. Res. Infect. Dis. Trop. Med 2, 1–8. https://doi.org/10.33702/ridtm.2020.2.1.1.

Sliz E Kalaoja M Ahola-Olli A, et al (2019). Genome-wide association study identifies seven novel loci associating with circulating cytokines and cell adhesion molecules in Finns. Journal of Medical Genetics 2019;56:607-616.

Smigal, C., et al. “Trends in Breast Cancer by Race and Ethnicity: Update 2006.” CA: A Cancer Journal for Clinicians, vol. 56, no. 3, 24 Feb. 2009, pp. 168–183., doi:10.3322/canjclin.56.3.168.

Smith SS, Buschang PH, Watanabe E, Interarch tooth size relationships of 3 populations: “Does Bolton’s analysis apply?”, American Journal of Orthodontics and Dentofacial Orthopedics, Volume 117, Issue 2, 2000, Pages 169-174.

Soh, J., Sandham, A. and Chan, Y.H. (2005) Occlusal status in Asian male adults: Prevalence and ethnic variation. Angle Orthodontist, 75, 814-820.

Soh, J., Sandham, A. and Chan, Y.H. (2005) Malocclusion severity in Asian men in relation to malocclusion type and orthodontic treatment need. American Journal of Orthodontics & Dentofacial Orthopedics, 128, 648-652. doi:10.1016/j.ajodo.2005.05.045

Sohlpour, A.; Jafari, A.; Pourhoseingholi, M.A.; Soltani, F. Corona COVID-19 virus and severe hypoxia in young patients without underlying disease: High prevalence rate with blood group A. Trends Anesth. Crit. Care 2020, 34, 63–64.

Solmaz, I.; Araç, S. ABO Blood groups in COVID-19 patients; cross-sectional study. Int. J. Clin. Pract. 2020, e13927.

Somogyi, Andrew A., et al. "Ethnicity-Dependent Influence of Innate Immune Genetic Markers on Morphine PCA Requirements and Adverse Effects in Postoperative Pain." Pain, vol. 157, no. 11, Nov. 2016, pp. 2458–2466., doi:10.1097/j.pain.0000000000000661.

Sushner NI. A photographic study of the soft-tissue profile of the Negro population. Am J Orthod. 1977 Oct;72(4):373-85. doi: 10.1016/0002-9416(77)90350-5. PMID: 269666.

Swlerenga D., et al. "Cephalometric values for adult Mexican- Americans". American Journal of Orthodontics and Dentofacial Orthopedics 106 (1994): 146-155.

Tang, E.L. (1994) Occlusal features of Chinese adults in Hong Kong. Australian Orthodontic Journal, 13, 159- 163.

Tang, E.L. (1994) The prevalence of malocclusion amongst Hong Kong male dental students. British Journal of Orthodontics, 21, 57-63.

Tuncay, Orhan C. "Matched, Equal, Equipoise." AJO-DO, American Journal of Orthodontics and Dentofacial Orthopedics, 1 Oct. 2015, www.ajodo.org/article/S0889-5406(15)00853-7/fulltext.

Tuncay, O. C. "Biologic elements of tooth movement." The Invisalign System. Quintessence; Berlin (2006).

Turley, P.K. Evolution of esthetic considerations in orthodontics, American Journal of Orthodontics and Dentofacial Orthopedics, Volume 148, Issue 3, 2015, Pages 374-379.

Uesato G., et al. “Steiner cephalometric norms for Japanese and Japanese Americans”. American Journal of Orthodontics 73 (1978): 321-327.

U.S. Department of Health and Human Services. “Bernadine Healy, M.D.” National Institutes of Health, U.S. Department of Health and Human Services, 3 Mar. 2017, www.nih.gov/about-nih/what-we-do/nih-almanac/bernadine-healy-md.

Van Alsten SC, Aversa JG, Santo L, Camargo MC, Kemp T, Liu J, Huang WY, Sampson J, Rabkin CS. Association between ABO and Duffy blood types and circulating chemokines and cytokines. Genes Immun. 2021 Jul;22(3):161-171. doi: 10.1038/s41435-021-00137-5. Epub 2021 Jun 8. PMID: 34103707; PMCID: PMC8185309.

Vardimon, A. D., Graber, T. M., & Voss, L. R. (1989). Stability of magnetic versus mechanical palatal expansion. European Journal of Orthodontics, 11(2), 107-115. doi:10.1093/oxfordjournals.ejo.a035971

Vardimon, A. D., Stutzmann, J. J., Graber, T. M., Voss, L. R., & Petrovic, A. G. (1989). Functional orthopedic magnetic appliance (FOMA) II—Modus operandi. American Journal of Orthodontics and Dentofacial Orthopedics, 95(5), 371-387. doi:10.1016/0889-5406(89)90299-0

Vardimon, A. D., Graber, T. M., Voss, L. R., & Mulfer, T. P. (1990). Functional orthopedic magnetic appliance (FOMA) III—Modus operandi. American Journal of Orthodontics and Dentofacial Orthopedics, 97(2), 135-148. doi:10.1016/0889-5406(90)70087-s

Vardimon, A. D., Graber, T., Voss, L. R., & Verrusio, E. (1987). Magnetic versus mechanical expansion with different force thresholds and points of force application. American Journal of Orthodontics and Dentofacial Orthopedics,92(6), 455-466. doi:10.1016/0889-5406(87)90227-7

Vardimon, A. D., Graber, T., Drescher, D., & Bourauel, C. (1991). Rare earth magnets and impaction. American Journal of Orthodontics and Dentofacial Orthopedics, 100(6), 494-512. doi:10.1016/s0889-5406(08)80004-2

Wang, X.F., Wang, Q., Ghasem-Zadeh, A., Evans, A., McLeod, C., Iuliano-Burns, S. & Seeman, E. (2009) Differences in macro- and microarchitecture of the appendicular skeleton in young chinese and white women. Journal of Bone and Mineral Research 24: 1946–1952.

Waters, Kevin M., et al. "Consistent Association of Type 2 Diabetes Risk Variants Found in Europeans in Diverse Racial and Ethnic Groups." PLoS Genetics, vol. 6, no. 8, 26 Aug. 2010, doi:10.1371/journal.pgen.1001078.

Wolpin, Brian M., et al. "ABO Blood Group and the Risk of Pancreatic Cancer." JNCI: Journal of the National Cancer Institute, vol. 101, no. 6, 18 Mar. 2009, pp. 424–431., doi:https://doi.org/10.1093/jnci/djp020.

Wong R. (2021). Inflammation in COVID-19: from pathogenesis to treatment. International journal of clinical and experimental pathology, 14(7), 831–844.

Woon, K.C., Thong, Y.L. and Abdul Kadir, R. (1989) Permanent dentition occlusion in Chinese, Indian and Malay groups in Malaysia. Australian Orthodontic Journal, 11, 45-48.

Wu, Y.; Feng, Z.; Li, P.; Yu, Q. Relationship between ABO blood group distribution and clinical characteristics in patients with COVID-19. Clin. Chim. Acta 2020, 509, 220–223.

Wu BB, Gu DZ, Yu JN, Yang J, Shen WQ. Association between ABO blood groups and COVID-19 infection, severity and demise: A systematic review and meta-analysis. Infect Genet Evol. 2020 Oct;84:104485. doi: 10.1016/j.meegid.2020.104485. Epub 2020 Jul 30. PMID: 32739464; PMCID: PMC7391292.

Wu J., et al. "Chinese norms of McNamara's cephalometric analysis". The Angle Orthodontist 77 (2007): 12-20.

Yaffe, A., Fine, N., & Binderman, I. (1994). Regional Accelerated Phenomenon in the Mandible Following Mucoperiosteal Flap Surgery. Journal of Periodontology, 65(1), 79-83. doi:10.1902/jop.1994.65.1.79

Yamamoto, F., Yamamoto, M., & Muñiz-Diaz, E. (2021). Blood group ABO polymorphism inhibits SARS-CoV-2 infection and affects COVID-19 progression. Vox sanguinis, 116(1), 15–17. https://doi.org/10.1111/vox.13004

Zalba Marcos S, Antelo ML, Galbete A, Etayo M, Ongay E, Garcia-Erce JA. (2020). Infection and thrombosis associated with COVID-19: possible role of the ABO blood group. Med Clin (Barc). S0025-7753(20):30443-30447.2712

Zeng X., Fan H., Lu D. (2020). Association between ABO blood groups and clinical outcome of coronavirus disease 2019: evidence from two cohorts. medRxiv.

Zhao, J., Yang, Y., Huang, H., Li, D., Gu, D., Lu, et al. (2021). Relationship Between the ABO Blood Group and the Coronavirus Disease 2019 (COVID-19) Susceptibility. Clin. Infect. Dis. 73 (2), 328–331. doi: 10.1093/cid/ciaa1150

Zietz, M., Zucker, J., & Tatonetti, N. P. (2020). Testing the association between blood type and COVID-19 infection, intubation, and death. medRxiv : the preprint server for health sciences, 2020.04.08.20058073. https://doi.org/10.1101/2020.04.08.20058073

Zylinski CG., et al. (1992). Analysis of soft tissue facial profile in white males. American Journal of Orthodontics and Dentofacial Orthopedics 101 (1992): 514-518.

APPENDICES

APPENDIX A

JOANNA BRIGGS INSTITUTE CRITICAL APPRAISAL TOOLS

JBI Critical Appraisal Checklist for
case control studies

Reviewer_____

Date_____

Author_____Year_____ Record Number_____

	Yes	No	Unclear	Not applicable
1. Were the groups comparable other than the presence of disease in cases or the absence of disease in controls?	□	□	□	□
2. Were cases and controls matched appropriately?	□	□	□	□
3. Were the same criteria used for identification of cases and controls?	□	□	□	□
4. Was exposure measured in a standard, valid and reliable way?	□	□	□	□
5. Was exposure measured in the same way for cases and controls?	□	□	□	□
6. Were confounding factors identified?	□	□	□	□
7. Were strategies to deal with confounding factors stated?	□	□	□	□
8. Were outcomes assessed in a standard, valid and reliable way for cases and controls?	□	□	□	□
9. Was the exposure period of interest long enough to be meaningful?	□	□	□	□
10. Was appropriate statistical analysis used?	□	□	□	□

Overall appraisal: Include □ Exclude □ Seek further info □

Comments (Including reason for exclusion)

_____

_____

JBI Critical Appraisal Checklist for cohort studies

Reviewer_____

Date_____

Author_____Year_____ Record Number_____

	Yes	No	Unclear	Not applicable
1. Were the two groups similar and recruited from the same population?	□	□	□	□
2. Were the exposures measured similarly to assign people to both exposed and unexposed groups?	□	□	□	□
3. Was the exposure measured in a valid and reliable way?	□	□	□	□
4. Were confounding factors identified?	□	□	□	□
5. Were strategies to deal with confounding factors stated?	□	□	□	□
6. Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?	□	□	□	□
7. Were the outcomes measured in a valid and reliable way?	□	□	□	□
8. Was the follow up time reported and sufficient to be long enough for outcomes to occur?	□	□	□	□
9. Was follow up complete, and if not, were the reasons to loss to follow up described and explored?	□	□	□	□
10. Were strategies to address incomplete follow up utilized?	□	□	□	□
11. Was appropriate statistical analysis used?	□	□	□	□

Overall appraisal: Include □ Exclude □ Seek further info □

Comments (Including reason for exclusion)

JBI Critical Appraisal Checklist for
systematic reviews and research syntheses

Reviewer_____

Date_____

Author_____Year_____ Record Number_____

		Yes	No	Unclear	Not applicable
1.	Is the review question clearly and explicitly stated?	□	□	□	□
2.	Were the inclusion criteria appropriate for the review question?	□	□	□	□
3.	Was the search strategy appropriate?	□	□	□	□
4.	Were the sources and resources used to search for studies adequate?	□	□	□	□
5.	Were the criteria for appraising studies appropriate?	□	□	□	□
6.	Was critical appraisal conducted by two or more reviewers independently?	□	□	□	□
7.	Were there methods to minimize errors in data extraction?	□	□	□	□
8.	Were the methods used to combine studies appropriate?	□	□	□	□
9.	Was the likelihood of publication bias assessed?	□	□	□	□
10.	Were recommendations for policy and/or practice supported by the reported data?	□	□	□	□
11.	Were the specific directives for new research appropriate?	□	□	□	□

Overall appraisal: Include □ Exclude □ Seek further info □

Comments (Including reason for exclusion)

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APPENDIX B

TABLE 1

Table 1. *Characteristics of Included Studies*

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Abdollahi et al (2020)	Iran	Retrospective case control	397 COVID-19 patients (cases) 500 controls	Controls 48.53 (17.9) Cases 58.81 (15.4)	Controls 46.2% M Cases 63.5% M	397 hospitalized patients (PCR+)	500 normal controls taken from Imam Khomeini hospital's blood bank database of patients before onset of the outbreak.	Investigate connection between ABO histo-blood group phenotype and COVID-19	Higher rate of infection was observed among patients with AB blood group while patients with O blood group showed a lower rate of infection. No association between severity of COVID-19 and ABO blood group phenotype	7 (Mod)	OR Infection Type A 1.16 (CI= 0.87-1.55) Type B 1.01 (CI= 0.72-1.42) Type AB 2.02 (CI= 1.17-3.51) Type O 0.68 (CI= 0.50-0.92) Severity Type A 0.96 (CI= 0.62-1.48) Type B 0.98 (CI= 0.59-1.64) Type AB 0.80 (CI= 0.37-1.72) Type O 1.17 (CI= 0.73-1.89)

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Ad'hiah et al (2020)	Iraq	Retrospective case control	300 hospitalized COVID-19 Iraqi patients (case) 595 healthy blood donors (control)	Cases 49.8±11.7 Controls 28.9±6.6	59.7% M	300 cases recruited from hospitals in Baghdad (had symptoms suggested of COVID and PCR+)	595 potential blood donors with serum that was negative for anti-virus antibodies	Understand genetic association of ABO blood groups with susceptibility to COVID-19 in Iraqi patients. Recovery and death were also explored.	AB and B+AB groups had increased risk to develop COVID-19 versus groups O No ABO associated risk was observed in recovered cases Increased risk of death with blood groups A, AB, A+AB, A+B+AB	5 (Low)	OR All cases vs controls Type O Reference Type A 1.46 (CI= 0.84-2.56) Type B 1.75 (CI= 0.98-3.13) Type AB 3.10 (CI= 1.59-6.05) Type A+AB 1.87 (CI= 1.12-3.12) Type B+AB 2.16 (CI= 1.28-3.63) Type A+B+AB 1.83 (CI= 1.14-2.94) Recovered cases vs controls Type O Reference Type A 0.76 (CI= 0.38-1.49) Type B 1.05 (CI= 0.55-2.02) Type AB 1.91 (CI= 0.91-2.00) Type A+AB 1.11 (CI= 0.62-1.96) Type B+AB 1.32

											(CI= 0.75-2.30) Type A+B+AB 1.09 (CI= 0.65-1.84) Deceased cases vs controls Type O Reference Type A 14.6 (CI= 2.85-74.88) Type B 2.07 (CI= 0.29-14.78) Type AB 12.92 (CI= 2.11-79.29) Type A+AB 14.67 (CI= 2.98-72.33) Type B+AB 6.30 (CI= 1.21-32.81) Type A+B+AB 9.67 (CI= 2.02-46.24)

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Ahmed et al (2020)	United Kingdom	Retrospective cohort	185 COVID- (Leicester), 84 COVID – (Birmingham), 86 COVID+	All F	Mean age COVID- group 31 Mean age COVID+ group 30	Pregnant women who were tested for COVID-19 and were +	Pregnant women at the same hospitals who were tested for COVID-19 and were -	Evaluate risk for COVID-19 in relation to ABO blood group	Blood group A women had a higher risk of developing COVID-19 infection. Blood group O had a lower risk.	6 (Mod)	Relative risk Type A 1.71 (CI= 1.05-2.78
Aljanobi et al (2020)	Saudi Arabia	Retrospective cohort	72 COVID-19 patients, 5291 blood donors (control)	33.3% M, 66.7% F	Mean age COVID patients 50 (36-58)	All hospitalized confirmed COVID-19 patients in QCH, eastern province, Saudi Arabia (PCR tested)	Blood bank registry for blood donors in the year 2019 to estimate distribution of ABO blood groups	Investigate relationship between ABO blood group and susceptibility to COVID-19 in patients at QCF (Qatif Central Hospital)	Higher susceptibility for group AB, lower susceptibility for group O	4 (Low)	OR Type A 1.00 (CI= 0.58-1.73) Type B 1.59 (CI= 0.97-2.61) Type O 0.52 (CI= 0.32-0.87) Type AB 2.64 (CI= 1.20-5.84)
Almadhi et al (2021)	Bahrain	Retrospective case control	4985 controls, 2138 cases	NR	NR	Random sample of COVID-19 positive individuals (PCR tested) who also had blood group data documented were selected from National COVID-19 Database 196 COVID-19 cases with ICU admission	Blood type of 4985 individuals who donated blood over the past two years in Bahrain were used as controls	Identify whether risk of COVID-19 infection and severity of clinical outcomes are associated with ABO blood groups and antibodies.	Higher risk associated with blood group B and lower risk associated with blood group AB. No association was observed between blood group and risk of severe ICU-requiring infection.	3 (Low)	OR Infection Type A 1.00 (CI= 0.89-1.13) Type B 1.17 (CI= 1.04-1.31) Type AB 0.69 (CI= 0.56-0.86) Type O 0.96 (CI= 0.87-1.06) ICU Type A 1.10 (CI= 0.76-1.56) Type B 1.14 (CI= 0.82-1.59) Type AB 1.14 (CI= 0.54-2.17) Type O 0.81 (CI= 0.60-1.11)

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Al-Youha et al. (2021)	Kuwait	Prospective cohort	3,305/3,730,027	Covid-19: 42.4±17.2 Controls: NR	Covid-19: 69.2% M, Controls: NR	SARS-CoV2 positive individuals using RT-PCR and admitted into the COVID-19 hospital	Anonymized individuals from national database	Examine blood group distribution in COVID-19 cohort and investigate relationship between blood group and clinical outcomes and compare blood group frequencies in COVID-19 cohort to the general population	No significant differences in severe clinical outcomes or death among the blood groups. Group A individuals had higher odds of developing pneumonia compared with non-A group Compared with general population, COVID-19 cohort had lower frequency of group O, equivalent frequency of A, higher frequency of B and AB.	7 (Low)	OR Pneumonia Type A=1.32, 95% CI= 1.02-1.72, p<0.036 Type B=0.85, 95% CI= 0.64-1.11 Type AB=0.93, 95% CI= 0.58-1.43 Type O=0.91, 95% CI= 0.71-1.17
Amoroso et al. (2021)	Italy	Retrospective cohort	265/56039	Case: 59.8 (11.9) Control: 56.4 (15.3)	Case: 72.8% M Control: 66.7% M	SARS-CoV-2 positive patients (molecular testing) who are also on transplant registry	Untested, asymptomatic counterparts	Comparing HLA and ABO frequencies according the presence or absence of SARS-CoV-2 infection	Group A was more frequent in COVID+ than COVID-	5 (Low)	Infection Blood group A OR=1.30, 95% CI=1.02-1.66 Death Blood group A OR=0.95, 95% CI=0.55-1.65

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Barnkob et al. (2020)	Denmark	Retrospective cohort	7422+/466232-/2204742 reference population	Case: 52 (40-67) Control: 50 (36-64)	Case: 32.9% M Control: 32% M	Positive RT-PCR for SARS-CoV-2	Participants who tested negative on RT-PCR test for SARS-CoV-2 Also used reference population with relevant blood group information from non-tested individuals	Status of ABO blood group and test results for SARS-CoV-2. Secondary outcomes hospitalization and death from COVID-19.	ABO blood groups varied significantly between patients and reference group with only 38.41% of the patients belonging to blood group O compared to 41.70% in the controls. ABO blood group is a risk factor for SARS-CoV-2 infection but not for hospitalization or death from COVID-19.	10 (Mod)	RR infection A RR= 1.09, 95% CI=1.02-1.13 B RR= 1.06, 95% CI=1.03-1.19 AB RR= 1.15, 95% CI=1.05-1.31 O RR= 0.87, 95% CI=0.83-0.91
Bhandari et al (2020)	India	Retrospective cohort	132 hospitalized COVID-19 patients compared with expected proportions of general population	M:F ratio 8:3	Mean age 36.68 yrs (SD=17.87)	132 hospitalized patients with COVID-19 (PCR tested)	Compared to expected proportions of ABO blood group distribution from a study of the North Indian population	Evaluate relationships between ABO blood group systems and susceptibility for SARS-COV2 infection	A Type is more susceptible to COVID-19	4 (Low)	Blood group phenotypes X^2= 0.23, p=0.890 A vs non-A X^2= 10.59, p=0.001
Boudin et al. (2020)	France	Retrospective cohort	1279/409	Case: 28 (23-36) Control: 27 (23-33)	Male 87%	SARS-CoV-2 infected subjected as defined by one positive RT-PCR (confirmed) and/or crewmembers with clinical symptoms highly suggestive of COVID-19	Participants in the same cohort who tested negative for COVID-19 and had no clinical signs	Relationship between ABO blood group and SARS-CoV-2 infection	ABO blood groups not associated with increased or decreased risk of infection by SARS-CoV-2	11 (High)	A OR= 1.06, 95% CI= 0.76-1.49, P= 0.73) B OR= 0.55, 95% CI= 0.29-1.07, P= 0.09) AB OR= 3.12, 95% CI= 1.6-6.03, P= 0.0017) O OR= 0.88, 95% CI= 0.63-1.23, P= 0.49)

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Chegni et al (2020)	Iran	Retrospective cohort	76 random samples of dead cases infected with SARS-COV2 Compared with 80,982,137 controls (from random study of blood group distribution)	<20, 1.1% 20-39, 7.4% 40-59, 38.3% >59, 53.2%	73 M, 21 F	Samples of dead cases infected with COVID-19	Controls in Iran from random study of blood group distribution	To determine whether there is an association between ABO blood type and COVID-19 infection	Those with blood group A are more likely to be infected with COVID-19	2 (Very low)	A X^2= 6.00, p=0.014 B X^2= 0.38, p=0.53 AB X^2= 1.38, p=0.23 O X^2= 3.03, p=0.082
Dutra et al. (2021)	Brazil	Retrospective cohort	430/2212	CCPD: 36.8±8.1 CIP: 69.3±15.7 Control: 37.5±12	CCPD: 61.6% M CIP: 63.6% M Control: 54.6% M	268 COVID-19 convalescent plasma donors and 162 COVID-19 in patients (confirmed by RT-PCR)	Healthy volunteer blood donors	Analyze association of SARS-CoV-2 infection with the presence of anti-A (in types O and B) or its absence (in types A and AB) related to the production of antibodies to SARS-CoV-2 nucleoprotein and neutralizing antibodies	Persons having types O or B showed less infection prevalence than those of types A or AB but no difference when COVID-19 in patients were analyzed. Immunoglobulins M, G, and A were lower in COVID-19 subjects of types O or B than those of A or AB	3 (Low)	O/B less infection prevalence OR=0.62, 95% CI=0.50-0.78 O vs B OR=0.66, 95% CI=0.46-0.95
Dzik et al (2020)	United States	Retrospective cohort	745 patients infected with COVID-19 at Massachusetts General Hospital, 212 from Brigham and Women's Hospital. 135 patients died	NR	NR	Non-survivors (PCR tested)	Survivors (PCR tested)	To determine whether there is an association between ABO blood type and COVID-19 mortality	Data does not support an association between ABO blood group polymorphism and fatality from COVID-19	8 (Mod)	For COVID-19, comparison of ABO distribution for survivors vs non-survivors X^2= 1.47, p = 0.688 Comparison of ABO among COVID-19 infected versus pre-COVID era patients X^2= 6.08, p=0.108

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Ellinghaus et al. (2020)	Italy and Spain	Retrospective case-control	1610/2295	NR	NR	Patients defined as hospitalization with respiratory failure and confirmed SARS-CoV-2 RNA PCR test	Blood donors without COVID-19	Morbidity and genomic analysis	Higher risk in blood group A as compared to other blood groups, protective effect of blood group O	2 (Very Low)	A vs non-A OR= 1.45, 95% CI = 1.20-1.75, P= 0.000148 O vs non-O OR= 0.65, 95% CI = 0.53-0.79, P= 0.0000106
Fan et al. (2020)	China	Retrospective case-control	105/103	Case: 56.8±18.3, Control :54.0±15.0	Case: 52.4% M Control: 54.4% M	Patients with PCR-RT confirmed COVID-19	Gender and age matched subjects with no other respiratory infections, infectious disease, or live and kidney dysfunction	Blood type frequency in case and control group, stratified by gender; relationship between ABO group and lymphocyte count	Significant association between blood type A and COVID-19 in the female subgroup but not in male	7 (Low)	OR (Gender stratified) Occurrence of COVID-19 Male Type A 1.14 (CI= 0.78-1.67) M Type B 0.93 (CI= 0.62-1.41) M Type AB 1.13 (CI= 0.63-1.98) M Type O 0.86 (CI= 0.53-1.4) Female Type A 1.56 (CI= 1.08-2.27) F Type B 0.85 (CI= 0.53-1.39) F Type AB 0.62 (CI= 0.24-1.61) F Type O 0.78 (CI= 0.48-1.26)

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Goker et al (2020)	Turkey	Retrospective case control	186 COVID positive individuals (cases) 1881 healthy individuals (controls)	Cases 42 (19-92)	Cases 53.8% M	186 patients from the Hacettepe Hospital who were positive for COVID-19 (PCR)	1881 healthy individuals who applied to the Hacettepe Blood Bank were included as controls.	Investigate the distribution and relationship between the blood groups amongst COVID-19 patients and their clinical outcomes.	Blood group A might have a role in increase susceptibility to COVID-19 infection and blood group O might be protective. However, once infected, blood group type does not seem to influence clinical outcome.	4 (Low)	OR Infection Type A 2.01 (CI= 1.50-2.90) Type B 1.40 (CI= 0.80-2.30) Type AB 1.30 (CI= 0.70-2.30) Type O 1.80 (CI= 1.20-2.50) Intubation A vs non-A 1.32 (CI= 0.37-4) AB vs non-AB 1.23 (CI= 0.10-10.40) O vs non-O 1.14 (CI= 0.20-4.50) ICU A vs non-A 1.03 (CI= 0.39-2.70) B vs non-B 1.03 (CI= 0.23-4.50) AB vs non-AB 2 (CI= 0.40-8.50) O vs non-O 1.16 (CI= 0.40-2.90) Mortality A vs non-A 2.73 (CI= 0.31-23.40) B vs non-B 5.01 (CI= 0.42-58.80) O vs non-O 2.72 (CI= 0.33-22.40)

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Golinelli et al. (2020)	Australia	Systematic review and meta-analysis	7 studies included (7503 COVID positive, 2,962,160 controls)	NR	NR	NR	NR	Investigate association between ABO blood groups and COVID-19 infection	SARS-COV2 positive individuals are more likely to have blood group A and less likely to have blood group O	10 (High)	Pooled OR Type A 1.23 (95% CI = 1.09-1.40) Type B 1.05 (CI= 0.96-1.26) Type O 0.77 (CI= 0.67-0.88) Type AB 1.09 (CI= 0.94-1.26)
Hoiland et al. (2020)	Canada	Retrospective cohort	95/398,671 (compared blood groups to national average) 38(A/AB)/57(O/B)	O/B: 66(58-73) A/AB: 71 (65-78)	O/B: 34 M A/AB: 27 M	ICU patients with RT-PCR confirmed COVID-19 infection	National database information from Canadian blood donors	Determine whether ABO blood group is associated with clinical indicators of COVID-19 severity, determine whether ABO blood group is associated with differences in serum biomarkers of organ dysfunction, assess whether ABO blood type is related to the levels of serum inflammatory cytokines	National and provincial ABO blood group distribution did not differ from COVID-19 cohort. Higher proportion of COVID-19 patients with blood group A or AB required mechanical ventilation CRRT, and prolonged ICU admission. Inflammatory cytokines did not differ between patients with blood group A or AB versus O or B	7 (Low)	Groups O/B vs A/AB Mechanical ventilation sHR= 1.76, 95% CI=1.17-2.65, p=0.007 CRRT sHR= 3.75, 95% CI=1.28-10.9, p=0.004 Extubation sHR= 0.92, 95% CI=0.52-1.62, Discharge from ICU sHR= 0.63, 95% CI=0.39-1.03 Died in hospital sHR= 1.22, 95% CI=0.47-3.21

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Hultstrom et al (2020)	Sweden	Retrospective cohort	64 COVID patients compared to blood type distribution in general population	Mean age A/AB group 63 years Mean age B/O groups 55 yrs	81% M A/AB group 69% M B/O group	Swedish critical care cohort	Blood type distribution in the general population	To determine whether blood type is associated with risk of requiring critical care or dying from COVID-19	Blood type A or AB is associated with increased risk of requiring critical care or dying of COVID-19 in the Swedish population	3 (Low)	Hazard ratio With requiring critical care Type A 2.01 (CI= 1.23-3.28) Increased risk of death within 30 days Type A/AB 3.16 (CI= 1.28-7.77)
Kibler et al (2020)	France	Retrospective case control	702 trans aortic valve replacement patients (22 with COVID-19 and 680 without)	82±6.9 (entire cohort) COVID-19 82±8.4 Non COVID-19 82±6.9	Entire cohort 44% M COVID-19 31.8% M Non COVID-19 45% M	22 TAVR patients with COVID-19 (PCR tested and used chest CT imaging to confirm). Severe cases were considered those who were hospitalized or died from COVID-19.	TAVR patients who did not have COVID-19	Investigate frequency and clinical course of COVID-19 in a large sample of patients who had undergone TAVR and to determine the associations of the ABO blood group with disease occurrence and outcomes.	Blood group A was the only independent predictor of COVID-19 in patients who had undergone TAVR. Blood group A was the only type significantly and independently associated with disease severity (hospitalization or death).	8 (Mod)	OR Occurrence of COVID-19 Type A 6.32 (CI= 2.11-18.92) Severe COVID-19 Type A 4.99 (CI= 1.64-15.27) Type O 8.27 (CI= 1.83-37.43)

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Latz et al (2020)	United States	Retrospective case control	7648 patients tested, 1289 tested positive with known blood type	Mean age: Blood Type A: 56.9 (18.6) Blood Type B: 57.6 (18.1) Blood Type AB: 57.1 (19.9) Blood Type O: 54.8 (18.1)	Blood Type A: 68% F Blood Type B: 67.7% F Blood Type AB: 54.1% F Blood Type O: 68.8% F	Patients with COVID-19 who presented to five major hospitals in the state of Massachusetts. 1289 patients were positive.	Hospitalized patients who tested negative.	Determine association between ABO blood type and severity of COVID-19 as defined by intubation or death as well as ascertain if there is variability in testing positive for COVID-19 between blood types	Blood type was not associated with risk of intubation or death. Blood type B and AB were associated with higher odds of testing positive for disease. Type O was associated with lower risk of testing positive.	10 (High)	OR Infection Type A 1.00 (CI= 0.88-1.13) Type B 1.28 (CI= 1.08-1.52) Type O 0.84 (CI= 0.75-0.95) Type AB 1.37 (CI= 1.02-1.83) Intubation/death Type A Reference Type B 0.72 (CI= 0.42-1.26) Type O 0.77 (CI= 0.51-1.16) Type AB 0.78 (CI= 0.33-1.87)
Leaf Karp et al. (2020)	United States	Retrospective cohort	2033/3.1 million	62 (52-71)	63.8% M	ICU patients with laboratory confirmed COVID-19 who also had ABO data available.	3.1 million blood donors in the United States	Examine relationship between blood group and clinical outcomes in patients with COVID-19	Blood type A may be a risk factor for COVID-19 related critical illness among white patients and type O blood may be protective No association with mortality	8 (Low)	NR
Lehrer et al. (2021)	United Kingdom	Retrospective cohort	12575 (5.7% COVID+)	58.8±8	48% M	COVID+ individuals (type of test not reported)	Participants who tested negative	Assess relationship of ABO locus to COVID-19 test positivity and mortality	No relationship found between blood group and COVID-19 test results	5 (Moderate)	NR

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Levi et al (2021)	Brazil	Retrospective case control	6457 patients who have been tested for COVID-19 1,813,237 (control)	NR	NR	6457 patients who have been tested for COVID-19 (4353 via PCR), 2275 (COVID antibodies) 171 (both). Most PCR+ patients were hospitalized.	1,813,237 patients from historical ABO blood group typing	Evaluate relationship between blood group types and SARS-COV2 laboratory results	No relationship between blood type and susceptibility to COVID-19	4 (Low)	NR
Li et al. (2020)	China	Retrospective cohort	265/3694	Case: less than 40 yrs (n=342), aged 41-59 yrs (n=784), over 60 yrs (n=1027) Control: NR	Case: 53.09% M Control: NR	Patients with COVID-19	The general healthy population	Relationship between ABO blood group and susceptibility and mortality of COVID-19 patients	Those with blood group A had significantly higher risk of SARS-CoV-2 infection whereas blood group O had lower risk	7 (Low)	ABO Blood Group Distribution A X^2=20.85 P<0.001 B X^2=0.95 P=0.329 AB X^2=1.83 P=0.176 O X^2=36.44 P<0.001 Deaths A X^2=0.22 P=0.639 B X^2=0.06 P=0.807 AB X^2=1.64 P=0.200 O X^2=2.16 P=0.141

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Liu et al. (2021)	China	Systematic review and meta-analysis	10 articles			Most studies included used COVID-19 diagnosis confirmed by RT-PCR	Most studies included used health blood donors as control	Investigate whether ABO blood groups are associated with increased COVID-19 morbidity and mortality	Increased odds of COVID-19 infection for blood group A compared to non-A blood group participants Slightly increased odds of COVID-19 infection for blood group B when compared to non-B blood groups Blood group O found to be protective Blood group A associated with significant increased risk of COVID-19 mortality	11 (High)	Infection A vs non-A OR=1.33, 95% CI= 1.14-1.56 B vs non-B OR= 1.06, 95% CI=1.00-1.13 AB vs non-AB OR= 1.07, 95% CI=0.88-1.30 Blood group O OR-0.71, 95% CI= 0.60-0.84 Mortality A vs non-A OR=1.25, 95% CI=1.02-1.52

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Mahmud et al. (2021)	Bangladesh	Prospective cohort	438 Covid +, Blood group A= 144, Blood groups B, O, AB= 294	39.8(13.2)	58.9% M	Patients with PCR-RT confirmed COVID-19 infection and blood group A	Patients with PCR-RT confirmed COVID-19 infection and blood group B, O, AB	Duration required for clinical improvement, proportion of patients converted to next level of severity, proportion of patients remaining positive for COVID-19 on day 14, development of post-COVID syndrome	Prevalence of blood group A significantly higher among COVID-19 patients than in general population ($p<0.001$). No differences observed between groups I and II in symptoms, severity. Persistent positivity of RT-PCR at 14 days was more frequent among patients with blood group A	9 (Mod)	Recovery within 7 days A vs non-A RR= 1.15, 95% CI = 0.93-1.42 Persistence of symptoms 12 or more days A vs non-A RR= 1.12, 95% CI = 0.81-1.55, Conversion to next level of severity A vs non-A RR= 1.49, 95% CI = 0.94-2.35, Persistent positivity A vs non-A RR= 1.71, 95% CI = 1.04-2.81, Post COVID syndrome A vs non-A RR= 1.25, 95% CI = 1.00-1.57

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Muniz-Diaz et al. (2020)	Spain	Retrospective cohort	854 (blood donors with mild COVID infection) and 965 (hospitalized), 75,870 (healthy blood donors), 52, 584 (uninfected patients who were transfused)	Covid-19 blood donors: 45.0 yrs (IQR 36.0-53.0) Healthy blood donors: 45.0 (32.0-53.0) Infected transfused patients: 69.0 (59.0-77.0) Uninfected transfused blood donors: 72.1 (58.2-82.5)	Covid-19 blood donors: 60.5% F, 39.5% M Healthy blood donors: 48.5% F, 51.5% M Infected transfused patients: 40.93% F, 59.07% M Uninfected transfused blood donors: 50.15% F, 49.85% M	Blood donors who had experienced mild COVID-19 infection (confirmed with RT-PCR) COVID-19 patients who were transfused during hospitalization	Blood donors who made their first donation in the first 4 months of 2020 Uninfected patient who were transfused at the same hospitals during the years 2019 and 2018	Verify association between ABO blood group and COVID-19 susceptibility and severity	Blood group A had higher risk and blood group O had lower risk for acquiring COVID-19 for the mild COVID-19 infection but this trend was not seen in the transfused groups Mortality risk in group A was significantly higher than group O.	6 (Mod)	Mild COVID OR Type A 1.23 (95% CI = 1.08-1.41) Type B 1.01 (CI= 0.79-1.31) Type O 0.78 (CI= 0.69-0.90) Type AB 1.20 (CI= 0.85-1.73) Transfused Patients (mortality or morbidity) OR Group A vs O 1.39 (95% CI = 1.06-1.89) Group A vs non-A 1.35 (CI= 1.03-1.78) Group O vs non-O 0.75 (CI= 0.56-0.99)
Niles et al. (2021)	United States	Retrospective cohort	34,178/242358	34.4 (29.2-40)	0% M	COVID+ on SARS-CoV-2 RNA NAAT as part of maternal screening process	COVID- on SARS-CoV-2 RNA NAAT as part of maternal screening process	Investigate association between ABO blood group with SARS-CoV-2 positivity by major race/ethnicity	Type O blood is protective (once adjusted for race/ethnicity)	5 (Low)	Infection Type O OR=0.95, 95% CI=0.92-0.99

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Pourali et al. (2020)	Iran	Systematic review and meta-analysis	139, 128 participants including 135,940 controls	NR	NR	NR	NR	Investigate association between ABO blood group and COVID-19 morbidity and mortality	Individuals with blood group A are at higher risk for COVID-19 infection while those with blood group O are at lower risk	9 (High)	Pooled OR Type A 1.16 (95% CI = 1.02-1.33) Type B 0.65 (CI= 0.23-1.84) Type O 0.73 (CI= 0.60-0.88) Type AB 1.25 (CI= 0.84-1.86)
Ray et al. (2020)	Canada	Retrospective cohort	225,556 patients who had ABO blood type assessed and COVID-19 testing. (7071 positive)	Mean age 53.8 yrs	29% M	Adults and children who had ABO blood group assessed and had positive COVID-19 testing (PCR)	Those who had ABO blood group assessed and tested negative on PCR	To determine whether ABO and Rh blood groups are associated with risk for SARS-COV2 infection and severe COVID-19 illness	O blood group may be associated with slightly lower risk for SARS-COV2 infection and severe COVID-19 illness	7 (Mod)	Adjusted RR for COVID-19 infection Type A 1.00 (reference) Type B 1.21 (CI= 0.13-1.29) Type O 0.95 (CI= 0.91-1.01) Type AB 1.15 (CI= 1.03-1.28 Adjusted RR for association between ABO and severe COVID-19 illness/death Type A 1.00 (reference) Type B 1.25 (CI= 1.07-1.45) Type O 0.93 (CI= 0.82-1.05) Type AB 1.27 (CI= 0.98-1.58 Adjusted RR for association

											between ABO and severe COVID-19 illness/death restricted to those who tested positive for COVID-19 Type A 1.00 (reference) Type B 1.04 (CI= 0.92-1.19) Type O 1.00 (CI= 0.90-1.10) Type AB 1.09 (CI= 0.88-1.33

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Sohlpour et al (2020)	Iran	Retrospective case control	93 hospitalized patients with hypoxia (case) compared to general population in Iran (control)	All younger than 45 yrs	NR	93 hospitalized ICU patients with hypoxia who were diagnosed as infected by COVID-19 (PCR+) and pattern of ground glass for COVID-19 in pulmonary CT scan. Patients has no underlying disease.	General population of Iran	Explore relationship between type of blood group and severe cases of hypoxia in young patients infected with COVID-19	Blood group A is more susceptible for involvement in severe COVID-19	1 (Very low)	In patients with hypoxia, 65% had blood group A, 23% AB, 8% had blood group B, 2% had blood group O. Compared to 36.49% (O), 32.09% (A), 23.68% (B), 7.74% (AB) in the general population
Solmaz et al (2020)	Turkey	Retrospective case control	1667 patients admitted to hospital with blood group information and positive covid test result (case) Data from blood group study with 127, 091 people (control)	NR	NR	1667 patients admitted to hospital with blood group information and positive PCR test result	Data from blood group study with 127, 091 people in Diyarbakir community	Investigate ABO and Rh blood group distribution and clinical characteristics in patients with COVID-19	Significant increase in number of individuals with COVID-19 who had blood type A and decrease in those with blood type O. For patients in need of intensive care and deceased patients, blood groups were not significantly associated.	4 (Low)	Blood group distribution Type A X^2= 20.59, p=0.000 Type B X^2= 0.001, p=0.979 Type O X^2= 34.19, p=0.000 Type AB X^2= 3.77, p=0.052 Intensive care Type A X^2= 0.53, p=0.465 Type B X^2= 0.63, p=0.424 Type O X^2= 0, p=0.99 Type AB

											X^2= 0, p=0.98 Death Type A X^2= 0.76, p=0.383 Type B X^2= 0.57, p=0.449 Type O X^2= 0, p=1.000 Type AB X^2= 0.003, p=0.959

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Wu et al. 1 (2020)	China	Retrospective case-control	187/1991	Case: over 40 years (n=116), less than 40 years (n=69) Control: NR	NR	Hospitalized patients with COVID-19	Patients who were hospitalized without COVID-19	Comparison of ABO blood group distribution between control and COVID-19 group; relationship between ABO blood group distribution and clinical characteristics of patients with COVID-19	Risk of COVID-19 for those with type A blood than in blood group O Risk of COVID-19 higher in patients with blood group A than any other blood group Patients with blood group O had lower risk of COVID-19 than patients with any other blood type	2 (Very Low)	A vs O OR= 1.84, 95% CI = 1.22-2.76, P= 0.003 A vs non-A OR= 1.54, 95% CI = 1.12-2.10, P= 0.006 O vs non-O OR= 0.649, 95% CI = 0.45-0.92, P= 0.018
Wu et al. 2 (2020)	China	Systematic review and meta-analysis	31,1000 samples included					Investigate relationship of ABO blood group with COVID-19 infection, severity, and demise	Those with blood group A had increased risk of COVID infection Those with blood group O had decreased risk of COVID infection Those with AB blood type had increased risk of severe COVID-19 Those with blood group A and blood group B have a trend of higher risk for severity	9 (High)	OR= 1.24, 95% CI=1.11-1.44 OR=0.69, 95% CI= 0.63-0.77 OR= 2.42, 95% CI=0.93-6.29 A OR=1.05, 95% CI=0.78-1.42 B OR=1.27, 95% CI=0.89-1.80 O OR=0.74, 95% CI=0.55-1.07

									Blood group A and AB associated with increased risk of death. However, blood groups O and B seemed to have higher mortality rate. No statistical significance.		

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Zalba-Marcos et al (2020)	Spain	Retrospective case control	226 COVID-19 patients compared to population ABO blood group distribution data	Mean age 70.9 yrs	Type A: 58.6% M Type B: 73.7% M Type AB: 80% M Type O: 66% M	226 COVID-19 positive hospitalized patients (PCR tested)	Population ABO blood group distribution data was extracted from the donor and transfusion management application	Describe distribution of the COVID-19 disease and its complications by blood groups in the population of Navarra and try to determine a possible relationship with ABO blood group	There was a significant association between thrombotic complications and admission to the ICU with blood group B developing more thrombosis and being admitted to ICU and group O being least admitted to ICU. More risk of developing other infections in groups A-AB.	6 (Low)	OR Respiratory Type A 1.22 (CI= 0.31-4.84) Type AB/B 1.01 (CI= 0.10-9.82) Type O Reference Thrombotic Type A Reference Type AB/B 6.16 (CI= 1.75-21.80) Type O 2.09 (CI= 0.67-6.54) Other infections Type A Reference Type AB/B 3.05 (CI= 1.11-8.39) Type O 2.36 (CI= 1.11-5.01)

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Zeng et al 2020	China	Retrospective case control	137 patients with mild pneumonia, 95 patients with severe pneumonia 500,000 Han Chinese (control)	56.8% M	Critical care cohort 67 (57-75) Mild cohort 52 (40-64(	PCR tested COVID + individuals Critically ill patients were defined as those admitted to ICU who required mechanical ventilation or had a fraction of inspired oxygen >60%	500,000 Han Chinese individuals as reference population	Examine correlation between blood type distribution and SARS-COV-2 infection progression and prognosis of COVID-19	Blood type A was more sensitive to SARS-COV-2. Blood type distribution was not relevant to acute respiratory distress syndrome (ARDS), acute kidney injury (AKI), and mortality in COVID-19 patients.	6 (Mod)	Adjusted OR Frequency Mild Cohort Type A 1.40 (CI= 1.01-1.96) Type B 0.70 (CI= 0.48-1.03) Type O 0.97 (CI= 0.69-1.36) Frequency Critical Cohort Type A 1.63 (CI= 1.10-2.42) Type B 1.00 (CI= 0.66-1.54) Type O 0.72 (CI= 0.47-1.13) ARDS Type A 1.31 (CI= 0.38-2.32) Type B 2.12 (CI= 0.55-8.15) Type O 1.00 AKI Type A 1.19 (CI= 0.29-4.90) Type B 1.89 (CI= 0.43-8.18) Type O 1.00 Death Type A 0.79 (CI= 0.19-3.20) Type B 1.20 (CI= 0.28-5.13) Type O 1.00

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Zhao et al (2021)	China	Retrospective case control	2173 COVID patients with 206 dead compared to 3694 non-COVID-19 from Wuhan and 23,386 non-COVID-19 from Shenzhen City	NR	NR	1775 patients infected with COVID-19 and 206 deceased cases (from the 1775) at Jinyintan Hospital in Wuhan Plus another 113 patients with COVID-19 from Renmin Hospital in Wuhan and 285 patients from Shenzhen Third People's Hospital in Guangdong (PCR tested)	Two recent surveys of ABO blood group distribution of 3694 non-COVID-19 from Wuhan and 23,386 non-COVID from Shenzhen were used as comparison	Investigate relationship between ABO blood type and susceptibility to COVID-19	Blood group A was associated with increased risk for both infection and death while blood group O was associated with decreased risk	3 (Low)	Jinyintan Hospital OR Infection Type A 1.27 (CI= 1.13-1.44) Type B 1.08 (CI= 0.95-1.23) Type O 0.68 (CI= 0.59-0.77) Type AB 1.11 (CI= 0.92-1.34) Deaths Type A 1.48 (CI= 1.11-1.97) Type B 0.96 (CI= 0.69-1.34) Type O 0.66 (CI= 0.47-0.91) Type AB 1.01 (CI= 0.62-1.64) Renmin Hospital Infection OR Infection Type A 1.39 (CI= 0.95-2.04) Type B 0.85 (CI= 0.54-1.34) Type O 0.64 (CI= 0.41-0.99) Type AB 1.53 (CI= 0.87-2.66) Shenzhen Hospital Infection OR Infection

											Type A 1.00 (CI= 0.77-1.29) Type B 1.22 (CI= 0.94-1.58) Type O 0.62 (CI= 0.48-0.81) Type AB 2.00 (CI= 1.42-2.82)

Table 1. (continued)

Study	Country	Study design	Sample Size (+/-)	Age	Gender	Patients	Controls	Outcomes	Findings	JBI	OR/RR/ES
Zietz et al (2020)	United States	Retrospective case control	14,112 adults with known blood type who tested COVID-19 +	A: 39% M AB: 41.3% B: 38.3% O: 38%	Mean age A: 58 (37-72) Mean age AB: 57 (37-71) Mean age B: 57 (37-72) Mean age O: 55 (36-71)	PCR tested COVID+ individuals	Used EHR data to compare blood types between COVID+ and COVID- groups	Evaluated associations between blood type and the following outcomes: infection prevalence and survival analysis for intubation and death	Adjusted prevalence showed higher prevalence for blood types A. AB, B than type O Blood type A was at decreased risk of intubation and death relative to type O. Type AB was at increased risk of both outcomes. Type B was at increased risk of intubation but lower risk of death compared with type O.	9 (High)	Effect Size (adjusted for race/ethnicity) Prevalence Type A 1.08 (CI= 0.98-1.19) Type B 1.08 (CI= 0.96-1.20) Type AB 1.01 (CI= 0.83-1.20) Intubation Type A 0.85 (CI= 0.68-1.03) Type B 1.12 (CI= 0.88-1.40) Type AB 1.09 (CI= 0.60-1.59) Death Type A 0.89 (CI= 0.71-1.12) Type B 0.83 (CI= 0.58-1.09) Type AB 1.10 (CI= 0.59-1.64)