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Original Research Article

Vaccines and Comorbidities: Balancing Risks and Benefits

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Vaccines have long been viewed as one of the most successful treatments in the history of public health.[1] They have helped to the elimination of various illnesses, including smallpox.[1,2] Vaccine hesitancy, or rejection or delay in immunisation, remains a substantial public health concern despite the obvious advantages of vaccination.[3]Vaccines date back to the 10th century when the Chinese started utilising variolation, a procedure in which material from smallpox abscesses was used to enter a healthy individual to prevent smallpox.[4] Even though this approach provided some protection for the illness, it was very dangerous and may have led to death or serious complications.[5] The modern age of vaccinations started with the efforts of Edward Jenner, who employed cowpox to produce protection against smallpox in the late 18th century. [5,6] This procedure, known as vaccination, was far safer than variolation and laid the groundwork for creating contemporary vaccinations. [5-7] Vaccines were produced throughout the following two centuries for various infectious illnesses, including measles, rubella, diphtheria, and polio. [7,8] These immunisations have reduced infectious disease-related morbidity and death.

The concept of herd immunity, which refers to protecting a community against infectious disease when a high percentage of the population is immune to the disease, was one of the most important developments in the history of immunisations.[1] This concept has considerably contributed to the efficacy of immunisations in managing and eradicating infectious diseases. [1,8]Despite the apparent benefits of vaccines, their creation and distribution have been contentious. Throughout history, there have been several vaccine scares and controversies, including the MMR (measles, mumps, and rubella) vaccine dispute in the 1990s, which caused a decline in vaccination rates and increased measles outbreaks.[1,9]In addition, the COVID-19 epidemic has highlighted the importance of immunisations in managing infectious diseases and the challenges connected with vaccine manufacture and distribution.[10]The rapid development and dissemination of COVID-19 vaccines was a significant achievement, and immunisations have played a major role in curbing the disease's spread.[11, 12]Vaccines stimulate an immune response against viruses or bacteria. As a result, the immune system creates a memory. This immunological memory allows the body to remember a specific virus or bacterium, enabling it to defend against and prevent the illness it causes. [13,14] Most vaccines include weakened or inactivated (killed)

viruses or bacteria or a minute quantity of disease-free viruses or bacteria. This is known as an antigen. [15,16]

The antigen is foreign to the immune system of a person who has received a vaccine. This activates the inflammatory reactions, allowing them to eliminate the invader and generate antibodies against it.[17, 18]Additionally, it activates T- and B-cells in the blood, bone marrow, and throughout the body.

The individual's immune system reacts to the genuine virus or bacterium if they meet it in the future.[19]The body may then swiftly produce the necessary antibodies and activate the immune cells to remove the virus or bacterium. This protects the individual against the disease.[20] Different vaccinations confer varying degrees of protection. The duration of protection also depends on the sickness being warded off. Some vaccinations only provide temporary protection against disease and may require booster doses; immunity might last a lifetime for others. [16,20]Vaccination protects more than only those who have gotten the vaccination. It indirectly protects unvaccinated community members, such as children too young to be vaccinated or those with compromised immune systems, by reducing the chance of infection exposure.[20,21]

This community immunity (herd immunity) requires sufficient immunised individuals.[21] In contrast, those who acquire immunity through contracting the disease risk exposing others to the illness and developing severe problems themselves.[20,21] Often, comorbidities, such as hypertension and diabetes, coexist with other disorders.

These diseases can substantially impact an individual's general health and well-being, as well as the efficacy of some treatments, such as immunisations.[22, 23] Hypertension, or high blood pressure, is a disorder that occurs when the stress of blood on the artery walls is consistently too high. This can lead to major health concerns like heart disease and stroke. Hypertensive individuals are at a greater risk for vaccination-related problems since their elevated blood pressure might place additional stress on the immune system.[24,25]Diabetes is a metabolic condition that impairs the body's use of sugar. Type 1 and type 2 diabetes are the two most common kinds of diabetes. Type 1 diabetes is an autoimmune illness in which the body attacks and kills the cells that create insulin.[26] Type II diabetes is a metabolic condition in which the body produces insufficient insulin or improperly responds to insulin. As diabetes can damage the immune system and make it more difficult for the body to fight off infections, people with diabetes are at a greater risk of developing problems from vaccines.[26,27]

Vaccines are intended to stimulate an immune response in the body to protect against certain diseases, such as viruses and bacteria. This immune response is a complicated process that involves several biomolecular alterations within the body. These modifications may involve activating numerous immune cells and the creation of particular macromolecules, such as cytokines, immunoglobulins, renin, and ACE.[28] Cytokines are a class of tiny proteins that are essential to the immune response. They serve as chemical signals to coordinate the immune response and are generated by various cells, including white blood cells. Some cytokines, such as interferons, assist in preventing the multiplication of viruses, while others, such as interleukins, aid in attracting and activating additional immune cells. Vaccination increases the production of cytokines, therefore protecting the body against infections.[29]

Immunoglobulins, commonly known as antibodies, are immune system proteins that identify and kill infections. Antibodies are created in response to vaccination and are particular to each disease. These antibodies are essential for pathogen defence because they prevent infection by attaching to the pathogen and tagging it for elimination by other immune cells.[27-29]Renin and ACE are enzymes involved in blood pressure control and fluid

balance. Renin is a kidney-made enzyme that transforms angiotensinogen into angiotensin I.ACE converts angiotensin I to angiotensin II, a vasoconstrictor that produces a rise in blood pressure. In reaction to vaccination, the production of renin and ACE can be elevated, leading to a rise in blood pressure. While this can be advantageous for the immunological response, it can harm those with hypertension.[30]

Vaccines and Glycemic Changes with Co-morbidities:

There have been reports of aggravation of hyperglycemia in diabetic individuals after receiving the CovishieldTM immunisation. One case report describes a hyperosmolar hyperglycemic condition following immunisation with the Pfizer-BioNTech COVID-19 vaccine. Immunisation appears to be the likely source of the abrupt spike in blood glucose levels. An immediate inflammatory reaction induced by the vaccination, in addition to an immunological response that manifested itself later, is most likely the cause of a little elevation that was only transient in the patients' blood glucose readings.[31] The cytokine storm, the steroids employed in therapy, and probably the direct beta cell damage caused by the virus are all to blame for these outcomes. The altered glucose metabolism has led to poor glycemic control in persons with diabetes and those who developed diabetes due to the epidemic. Exploration of the many routes through which SARS dysregulates glucose metabolism is essential for understanding the disease. (Mishra et al., 2021).[32]

The CDC recommends the COVID-19 vaccination for patients with type 1 and 2 diabetes. The Johnson & Johnson vaccination is indicated for anyone older than 18 years. Diabetes types 1 and 2 increased the likelihood of developing COVID-19 symptoms. This is related to the vaccine-induced mild, transient irritation. Milder effects, such as arm soreness and weariness, subside 24 hours after vaccination. Priority should be given to administering COVID-19 immunisation to those with type 2 diabetes. Type 2 diabetes can develop from various causes, including a poor diet and lack of exercise.[32] The CDC's Vaccine Adverse Effect Reporting System contains more than 350 cases of hyperglycemia following influenza vaccination. Four mornings and 24 hours following immunisation, glucose levels were measured. Before receiving a single dose of vaccine, the researchers evaluated the subjects' haemoglobin A1c and glucose levels.[34]

A 41-year-old Caucasian man with a history of type 2 diabetes and no microvascular complications received a trivalent inactivated influenza vaccine (Seqirus Pty Ltd., Parkville, Victoria, Australia). Two hours after vaccination, he reported feeling fatigued and groggy, and his blood glucose level was 264 mg/dL. The influenza vaccination produced a significant hyperglycemic impact that normalised after 72 hours without intervention. Physiological stress, such as that caused by surgery, infection, injury, or severe sickness, can potentially elevate counterregulatory hormone levels. People with diabetes cannot quickly offset such blood glucose rises (Glaess et al.).[35]

Co-morbidities and Post-Vaccination Cytokine and Immunoglobulin Titers:

Antibody titers of the A/Chile, A/Philippines, and B/USSR anti-influenza vaccinations recommended by the WHO increased significantly (p 0.01) among diabetic individuals with Type 1 and Type 2 diabetes. Four twenty-one diabetes individuals lacked an antibody response against all three virus types. The results indicate that people with type 1 and type 2 diabetes can acquire good protection against the influenza virus.[34]

People with type 2 diabetes (T2DM) showed substantially lower IgG and neutralising antibody titers in response to two doses of the Pfizer-BioNTech BNT162b2 mRNA vaccine

than those without diabetes. Age, gender, BMI, and hypertension did not influence antibody titers significantly (Ali et al., 2021). [36]

Glucose metabolism plays a crucial role in the influenza-associated cytokine storm. The association may have consequences for emerging coronavirus infections. Researchers suggest inhibiting a critical enzyme in the glucose cycle might be one approach to avert a fatal storm. Chinese and German virologists have uncovered how the activation of a glucose metabolism pathway by influenza results in an out-of-control immunological response. Interfering with this system may be one method to avoid the cytokine storm observed during influenza and other viral illnesses. To activate the host's stress response to a viral infection, the OGT enzyme is necessary. According to experts, interfering with this metabolic route might prevent the cytokine storms seen in severe instances of influenza or COVID-19. Individuals with type 2 diabetes are more prone to severe influenza infections (Lewis, n.d.) [37]

During immunisation time, poor glucose management may impede immune responses. Patients with HbA1c levels above 7% had decreased neutralising antibody titers and CD4 cytokine responses involving type 1 helper T cells 21 days after the first vaccination injection. Similar rates of virus-neutralizing antibodies and antigen-specific CD4-cell responses were seen in patients with and without diabetes.[38]

Inadequate glycemic management during vaccination may diminish the efficiency and duration of SARS-CoV-2 protection. There was a 1.3-fold decrease in CD14+ monocytes in T2D patients. There were no differences in the immune responses induced by the several SARS vaccines tested. Data about coronavirus disease 19 (COVID-19) vaccines are sparse. Included were 555 elderly residents of LTCFs who participated in the GeroCovid Vax research. Using chemiluminescent assays, SARS-CoV-2 trimeric S immunoglobulin G (anti-S IgG) concentrations were measured before the first dosage and after 2 and 6 months (Virgilio et al., 2022).[39]

The research involved 101 healthcare professionals who received two doses of an inactivated virus vaccination (CoronaVac). Interviews and physical examinations collected data on demographic profiles, medical histories, and clinical parameters. A history of hypertension and high blood pressure were substantially linked with reduced antibody titers. (Hypertension is related to antibody response and re-infection following vaccination with inactivated SARS-CoV-2 in healthcare workers, 2022) [40]

Post Vaccination – ACE changes with comorbidities:

Diabetes is linked to an increased risk of complications from various illnesses; COVID-19 is not an exception to this rule. People who have diabetes, particularly those who have diabetes-related kidney impairment, frequently have ACE2 enzymes that are either hyperactive or expressed too early in their bodies. The amplification of these enzymes can lead to difficulties on their own, but the risk of complications is significantly increased when a virus is present. It is well-established that COVID-19 can lead to serious lung, heart, and kidney issues. This may be related, at least in part, to the high level of activity that ACE2 cells have in these tissues in persons with the virus. People with higher ACE activity have more host sites where the virus may attach itself once it has entered their systems (Diabetes and COVID-19: The ACE2 Connection, n.d.).[41] The possible role that complement factors might have in protective immunity against SARS-CoV-2 has been largely neglected by researchers. Multiple functions, including innate and adaptive responses, are performed by complement in the immune system. There is not enough information available at this time to substantiate either the function complement inhibitors play or their advantages. Researching the significance of antibody–complement interactions in viral neutralisation and immunity is

necessary. (Kurtovic and Beeson, 2020) [Kurtovic and Beeson][42] Evidence from clinical studies suggests that the complement system may play a significant role in developing COVID-19.

Although this is an exciting discovery, it is important to proceed with care for now. It is expected that complement-targeting medicines will show promise in human trials but that their efficacy will be contingent on various confounding factors, such as the severity of the disease and the point in time when treatment was first initiated (Afzali et al., 2021).[43]

To successfully emerge from the present phase of the pandemic, COVID-19 immunisation proved to be the most effective technique. Vaccines against SARS-CoV-2 have recently come under scrutiny for several potential safety issues. It is possible for free-floating Spike proteins that have been released by damaged cells to connect with the ACE2 of other cells, leading to the increased likelihood of ACE2 being internalised and degraded. This method may contribute to an even greater imbalance between the overactivity of Ang II and the lack of Ang1-7 by reducing the activity of the ACE2 receptor (Angeli et al., 2022).[44,45]

1. CONCLUSION:

In conclusion, while there is a growing body of research on the impact of vaccines on biomolecular changes in individuals with comorbidities, such as hypertension and diabetes, very few cases are reported in the literature. This highlights the need for further research to understand better how these conditions may affect the immune response to vaccines. However, it should be noted that vaccines are still considered safe and effective in preventing serious infectious diseases in people with comorbidities. It is important for individuals with comorbidities to talk to their healthcare provider about their risk of complications and to make sure they are up to date on all recommended vaccinations. This is crucial because these individuals are at increased risk of vaccination complications. They should also manage their comorbidities properly and maintain a healthy lifestyle, including regular exercise, a balanced diet, and stress management. This can help improve overall health and reduce the risk of vaccination complications. It is also important to note that the lack of evidence of biomolecular changes after vaccination in patients with comorbidities does not mean that the vaccine is not working; it can be that the changes are not noticeable or that the research is not yet available. Vaccines have been proven effective in preventing serious infectious diseases, and the benefits far outweigh the risks. In addition, it is important to remember that vaccines are continuously being researched and developed. More information about the impact of vaccines on biomolecular changes in individuals with comorbidities may become available. Therefore, staying updated with the latest research and recommendations from healthcare providers is important.

In summary, vaccines are still considered safe and effective in preventing serious infectious diseases in people with comorbidities, despite the limited evidence of biomolecular changes after vaccination in these patients. It is important for individuals with comorbidities to talk to their healthcare provider about their risk of complications and to make sure they are up to date on all recommended vaccinations. Proper management of comorbidities and maintaining a healthy lifestyle can also help reduce the risk of complications from vaccinations, as inferred from the above research articles.

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