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Pharmacosurviellance On Covid Vaccine-An Adverse Event Following Immunization(Aefi) Study At Guntur District

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I. INTRODUCTION

Vaccine is responsible for the worldwide eradication of smallpox and the restrictionof diseases such as polio, measles, and tetanus from much of the world. The effectiveness of vaccination has been widely studied and vaccine typically contains an agent that resembles a

disease-causing microorganism and is often made from weakened or killed forms of the microbe, its toxins, or one of its surface proteins. The agent stimulates the body's immune system to recognize the agent as a threat, destroy it, and to further recognize and destroy any other microorganisms associated with that agent that it may encounter in the future. A vaccine is a biological preparation that provides active acquired immunity to a particular disease. These are prophylactic (to prevent or ameliorate the effects of a future infection by a natural or "wild" pathogen), or therapeutic (e.g., vaccines against cancer, which are being investigated). The administration of vaccines is called vaccination. Vaccination is the most effective method of preventing infectious diseases; widespread immunity due to vaccination is largely verified; for example, vaccines that have proven effective include the vaccine, the HPV vaccine, and the vaccine. The World Health Organization (WHO) reports that licensed vaccines are currently available for twenty-five different preventable infections.[1]

The terms vaccine and vaccination are derived from *Variolae vaccinia* (smallpox of the cow), the term devised by Edward Jenner to denote cowpox. He used it in 1798 in the long title of his Inquiry into the *Variolae vaccinia* known as the cow pox, in which he describedthe protective effect of cowpox against smallpox. In 1881, to honor Jenner, Louis Pasteur proposed that the terms should be extended to cover the new protective inoculations then being developed[1].

Vaccine design:

It concerns the selection of antigens, vaccine platforms, and vaccination routes and regimen.The choice of vaccine platform determines the relative immunogenic strength of vaccine-derived viral antigens, whether an immune adjuvant is required and the nature of protective immunity. These attributes also determine the suitability of a vaccine fora particular route of vaccination, and whether a prime–boost vaccination regimens requiredto increase vaccine- mediated protective immunity and its durability. Furthermore, the selection of live attenuated viral vaccines or a respiratory mucosal route of vaccination will require more stringent safety testing[1].

Vaccine platforms

In general, vaccine platforms are divided into six categories: live attenuated virus, recombinant viral- vectored vaccines that are bioengineered to express target pathogen antigens in vivo, inactivated or killed virus, protein subunit vaccines, virus- like particles(VLPs) and nucleic acid- based (DNA or mRNA) vaccines .In broad terms, vaccines require two components :antigens from the target pathogen that are provided to or generated by the vaccine recipient; and an infection signal (such as a pathogen- associated molecular pattern or damage- associated molecular pattern) that alerts and activates the host immune system. Live attenuated vaccines can naturally provide both of these components, whereas non- viral vaccine platforms can provide the antigens but often require the artificial provision of signals to alert the immune system known as adjuvants[2].

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 525-547 www.ijprajournal.com ISSN: 2456-4494

Vaccination routes and regimens

In addition to the careful selection of vaccine antigensand platform, the route of vaccination is an integral consideration of vaccine strategies. This is particularly important for mucosal pathogens such as SARS- CoV-2 and those pathogens against which optimal protection requires not only neutralizing antibodies but also innate and adaptive cellular immunity. The best window of opportunity for SARS- CoV-2 control and clearance is the asymptomatic or

pre symptomatic period of COVID-19 (2–12 days), which is likely to require all of the immune protective elements to be present within the respiratory mucosa before viral entry. The route of vaccination has a crucial role in determining this. Protective IgG antibodies induced by parenteral vaccination readily appear at the respiratory mucosa, this being the primary mechanism by which intramuscular injection of measles or influenza vaccine offers protection in humans. However, this route of vaccination is unable toeffectively induce mucosal IgA antibodies or TRM cells in the lungs. By comparison, the respiratory mucosal route of vaccination is adept at inducing antibodies and TRM cells in the respiratory mucosa, as well as macrophage- mediated trained immunity. Inactivated virus, protein subunit and nucleic acid vaccines cannot be administered by the respiratory mucosal route owing to their requirement for potentially unsafe immune adjuvants and repeated delivery. By contrast, recombinant viral- vectored vaccines, particularly those using humanizer type 5 adenovirus (Ad5) or chimpanzee- derived adenovirus (ChAd), are safe and highly effective for respiratory mucosal vaccination. Often, weakly immunogenic vaccines based on inactivated virus, protein subunits, nucleic acids or viral vectors such as Ad26 require a repeated homologous vaccination regimen to be effective. Indeed, most current human vaccines require repeated doses. As It is not yet known which COVID-19 vaccine strategy will be used or for how long the vaccine- induced protection may last in humans, it remains possible that a homologous or heterologous prime–boost vaccination regimen will be required to sustain protection, even with robust stand- alone platforms such as ChAd. The same or a different route may be used for the repeated vaccine delivery. vaccines that entered clinical trials in China, the UK and the USA in mid- March 2020. Clinical trials for the remaining 24candidates are currently recruiting volunteers and a couple of other candidates are also about to enter clinical trials. Preclinical evaluation of candidate vaccines requires the use of relevant animal models of COVID-19. Conventionally, the safety, immunogenicity and protective efficacy of experimental vaccines are rigorously evaluated and established in animal models first before clinical trials are begun. In the case of pandemic vaccine development, however, the preclinical and clinical stages of vaccine development are compressed and move forwards in parallel[3].

As a consequence, immunization coverage in Italy has decreased both in children and adults in recent years. Compulsory vaccination for children, therefore, became enacted into Law in July 2017 in order to address the vaccination short fall in Italy. Consequently, the number and uptake of compulsory vaccination have increased from 4 to 10. These are those included in the hexavalent vaccine (diphtheria, tetanus, pertussis, poliomyelitis, hepatitis B, and hemophilus influenza B) and measles, mumps, rubella, and varicella, for children up to 6 years of age to be enrolled in kindergartens and pre-schools and for children up to 16 years ofage to attend compulsory schools.

Furthermore, health authorities are requested to promote all vaccines (mandatory and non-mandatory) recommended in the 2017–2019 National Immunization plan. As a matter of fact, vaccines such as those against Neisseria meningitidis, Streptococcus pneumoniae, or human papilloma virus are not included in the mandatory vaccination law; however, they are included in the recent Italian National Vaccination Plan (2015–2017) and are given free of charge to all newborn (Neisseria meningitidis and Streptococcus pneumoniae) or to all adolescents, both male and female (HPV vaccine)[4].

TYPES OF VACCINES

Live attenuated viral vaccine

Historically, several successful human vaccines, such as measles vaccine and the bacillus Calmette–Guérin (BCG) vaccine for tuberculosis (TB), havebeen based on attenuated strains of the actual pathogen, with loss or mutation of viral genes through in vitro passage. It is now possible to rationally design attenuated virus strains by mutating or deleting virulence genes. This deletion mutant scan often replicates toa limited extent in host cells but lose the ability to cause disease in vivo. Corona viruses shave several genes that are not required for replication and that can be deleted, leading to attenuation in vivo. Deletion of various non- structural proteins, as well as of the structural E protein, has been used as a strategy to engineer

international Journal of Pharmaceutical research and Applications
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vaccine strains of several zoonotic and veterinary coronaviruses. Deletion of the E protein leads to attenuation and generation of an efficacious vaccine strain, but reversion of the attenuated phenotype therefore provides a preferred mechanism of attenuation. For example, deletion of the 2′- *O*-methylase gene from the SARS- CoV genome removes the ability of the virus to hide its RNA from the host cell proteins MDA5 (also known as IFIH1) and IFIT1, thereby inducing a robust antiviral response in vivo. Another approach to viral attenuation is known as codon deoptimization, whereby the nucleic acid sequence is modified to use sub optimal codons to encode the wild- type amino acid sequence which considerably slows the translation of the viral protein during infection. This approach can yield a virus that is highly attenuated in vivo but still able to replicate in vitro if the correct viral protein is selected for deoptimization. However, the generation of an attenuated strain of a pathogen for use as a vaccine requires demonstration of its inability to revert genetically to become pathogenic. This is particularly challenging in the case of coronaviruses as they are known to recombinein nature, and an attenuated vaccine strain could, in theory, recombine with wild coronaviruses to recreate a pathogenic strain. So far, there are only three attenuated SARS- CoV-2 vaccines generated by codon deoptimization under preclinical development, by Mehmet AliAydinlar University in Turkey, Codagenix and Serum Institute of India, and Indian Immunological Ltd and Griffith University[5].

Recombinant viral- vectored vaccines

Recombinant viral- vectored vaccines are built on either a replication deficient viral backbone or an attenuated replication competent viral backbone that is bioengineered to express antigens derived from the target pathogen. Although only a couple of viral- vectored vaccines have been approved for human use for thecontrol of infections such as Ebola, this platform has been widely investigated and has a well-established track record for infectious diseases and cancer, given its genetic malleability, safety and ability to induce strong T cell responses without the need for an adjuvant. Some viral vectors, such as Ad5 and ChAd, usually need to be administered only once for protection and have natural tropism for the respiratory mucosa, which means they are amenable to respiratory mucosal vaccination. The technology already exists for their large- scale clinical grade production and storage[5].

Inactivated viral vaccines

Physically or chemically inactivated viruses have been used successfully in human vaccines against polio, hepatitis A and influenza. Inactivated viruses can be rapidly generated and scaled up in a pandemic situation using well-established infrastructure and methods. Inactivated viral vaccines have few safety concerns, unlike their live attenuated counter parts, and they express a wide range of native viral antigens, includingsurface antigens with retained epitope conformations that can induce conformation- dependent antibody responses. Currently, there are five early clinical trials to assess inactivated SARS- CoV-2 vaccines, with an additional nine candidates in preclinical development. PiCoVacc, an inactivated SARS-CoV-2and alum- adjuvanted vaccine developed by Sinovac Biotech Ltd in China, is the most advanced candidate with published preclinical results. It protects rhesus macaques against SARS- CoV-2, with reduced viral titersand immunopathology associated with antibodies to S protein and nucleo capsid. BBIBP- CorV, another inactivated virus candidate, which is being developed by Chinese state- owned Sino pharm, was tested in arrange of animal models, with demonstrated efficacy in non-human primates. Although these findings provide optimism, the observations were made in rather short- term studies and should be interpreted with caution. The use of alum as an adjuvant makes them unsuitable for respiratory mucosal delivery. Although the protection mediated by intramuscular immunization with PiCoVacc or BBIBP- CorV indicates some level of mucosal immunity, probably through the transport of systemic antibodies to the lungs, the durability of such immunity remains unclear as SARS- CoV-2 challenge was performed 1–4 weeks after vaccination. Furthermore, similarly to protein subunit vaccines, inactivated viral vaccines are poor inducers of cytotoxic CD8+ T cells, which are likely to be required for an effective COVID-19 vaccine[6].

Protein subunit vaccines

Currently, there are sevenCOVID-19 subunit vaccines in clinical trials, with 50 other candidates under preclinical development, making this the most common platform. Subunit vaccines primarily induce CD4+ TH cell and antibody responses. Therefore, most of these vaccines contain full- length SARS- CoV-2 S protein or portions of it with the goal of inducing neutralizing antibodies, similarly to the majority of SARS and MERS vaccines, which had differing levels of efficacy.

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Subunit vaccines canbe designed to focus the immune response towards neutralizing epitopes, there by avertingthe production of non- neutralizing antibodies that may promote ADE of disease. However, unlike nucleic acid- based or viral-vectored vaccines, recombinant S proteins in subunit vaccines could have an improper epitope conformation unless they are produced inmammalian cells. Proteins or peptides alone are poorly immunogenic and generally require not only an adjuvant but also repeated administration, and they are poor activators of CD8+ T cell responses. Furthermore, this platform is generally unsuitable for respiratory mucosal vaccination. As is the case for inactivated viral vaccines, use of unmodified alum as an adjuvant skews the immune response towards TH2 cell- like responses, which is undesirable for host defense against SARS- CoV-2 and may have a role in ADE of disease in this regard, subunit COVID-vaccines being developed by GlaxoSmithKline and Novavax use AS03 an Matrix- M adjuvants, respectively.

Virus- like particles

VLPs are spontaneously forming particles composed of several structural viral proteins that are co- expressed or admixed. Several commercial vaccines, suchas hepatitis B and human papilloma virus vaccines, are based on VLPs. In the case of enveloped coronaviruses, VLPs form when the viral proteins S, Mand E, with or without N, are co-expressed in eukaryotic producer cells. This results in active budding from the producer cells of VLPs that are structurally identical to the infectious virus but lack the viral genome and thus are non-infectious. The presence of S protein on the surface of VLPs enables them to bind and enter ACE2+cells in the same manner as the parent virus. Unlike subunit vaccines, the array of S protein on the VLP surface crosslinks the B cell receptor and directly activates B cells, but, like subunit and inactivated viral vaccines, VLPs also typically require an adjuvant and repeated administration. Notwithstanding this, the VLP technology is well established, the biology and safety of coronavirus VLPs are understood and their large- scale production to Good Manufacturing Practice standards is relatively straight forward. Currently, there is only 1 VLP- based COVID-19vaccine in clinical trials , with 12 more under preclinical development. These are produced either in vivo from a viral vector, such as MVA, that expresses the VLP components (a platform being developed byGeoVax) or more often in vitro from producer cells[7].

Nucleic acid- based vaccines

Recombinant plasmid DNA has been explored as a vaccineplatform for decades, whereas mRNA has emerged more recently as a promising platform.Currently, there are 6 mRNA-basedCOVID-19 vaccines and 4DNA- based COVID-19vaccines in clinical trials, with 27 such vaccines (16 mRNA- based and 11 DNA- based vaccines) under preclinical development. The antigen encoding mRNA complexed with a carrier such as lipid nanoparticles can be efficiently delivered in vivo into the cytoplasm ofhost cells for protein translation and post- translational modifications, which is an advantageover recombinant protein subunit vaccines. mRNA vaccines are non- infectious and aresynthesized by in vitro transcription, free of microbial molecules. These beneficial featuresdifferentiate mRNA vaccines from live attenuated viral vaccines, inactivated viral vaccines,subunit vaccines and recombinant viral- vectored vaccines in terms of safety ,efficacy andissues of antivector immunity, enabling their rapid and inexpensive production andrepeatedvaccination.mRNA- 1273, which is produced by Moderna, an American biotechcompany that has experience with mRNA-based MERS vaccines, encodes a pre fusionstabilized SARS- CoV-2 S protein encapsulated in lipid nanoparticles. It entered clinicaltesting even before the release of preclinical data. Recently published phase I clinical trialdata indicate that low and medium doses of two repeated parenteral injections are generallysafe and induce strong S protein- specific antibody responses and a primarily CD4+ T cellresponse in most trial participants. Pfizer and BioNTech are also assessing an mRNA–lipidnanoparticle vaccine encoding the developed robust S protein- specific antibody andCD4+and CD8+ T cell responses following two repeated parenteral injections. ThePfizer/BioNTech and Moderna vaccines have both been selected for US Operation Warp Speed.[8]

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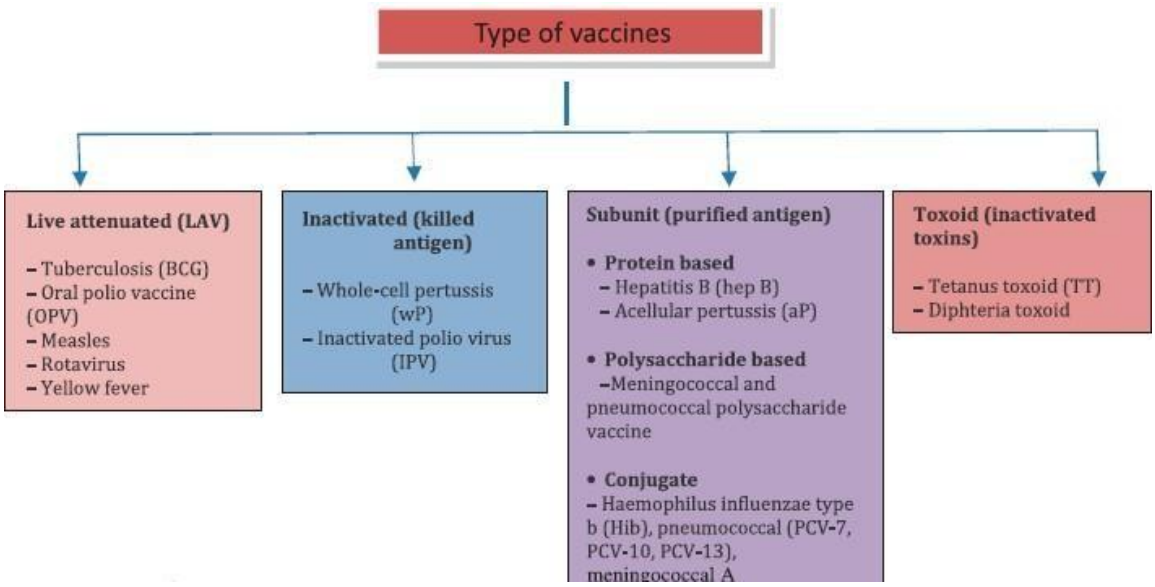

Fig:1.1 Types of Vaccines

COVID

The pandemic namely corona virus is rapidly out breaking from its primary source from the city of wuhan, situated in china to the entire world (1, 2). This disease is a serious outbreak to the rest of the countries, resulting in damaging effect to the human body. This article gives broad spectrum of view for the pandemic disease. Firstly, in the monthof December 2019, many patients of unspecified etiology of pneumonia which all had a history of visit to seafood whole sale market in Wuhan, China (SARS-COV-2) in month of February 11, 2020. The virus causing this pandemic disease is termed as COVID-19 by the world health organization on 11th February 2020 (3, 4). Recently, Corona virus has become a critical condition of international concern of public health, WHO stated its danger to the extreme highest level. This virus has damaging effects over various human organs like lungs, can disrupt cardiac function by affecting the heart, may lead to renal problem by affecting the kidneys, hepatic dysfunction, and also affect genital organs of the human body (5, 6). Going through the literature the patients, who all were tested positive for COVID-19, ultimately lead towards acute respiratory distress syndrome (ARDS) in 67.3% of cases, acute kidney injury in 28.9% of cases, disrupted hepatic function in 28.9% of cases and cardiac injury in 23.1% of cases and on the 28th day mortality rate was 61.5%.[7]

HISTORY

It is a RNA virus with diameter ranging from 60nm to 140nm having projectionssimilar to spike on the superficial surface which give its appearance of crown under an electron microscope. There have been two events in the past two decades wherein crossover of animal beta corona viruses to humans has resulted in severe disease. The very first occurrence of the virus was in 2002-2003, when a virus from β genera with its prime origin from bats, crossed over to humans via mediator host of cats from Guangdong province of the country China. This virus cause infection to 8422 people mostly in the country China along with Hong Kong and resulted in 916 deaths with a mortality rate of 11% before being contained and is designated as severe acute respiratory syndrome corona virus. Almost a decade later in 2012, the Middle East respiratory syndrome coronavirus (MERS-CoV), also of bat origin, emerged in Saudi Arabia with dromedary camels as the intermediate host and affected 2494 people and caused 858 deaths (fatality rate 34%).[8]

PATHOGEN

SARS-CoV-2 is an animal virus that belongs to the b- coronavirus genus. Current studies showed that bats, snakes, and pangolins may be the hosts for SARS-CoV- 2. Result of genetic sequencing shows that bats are the primary host for corona virus as the homology between two coincides 96% (16) but the intermediate host for the same virus is still unknown.[8]

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 525-547 www.ijprajournal.com ISSN: 2456-4494

GENETIC STRUCTURE AND PATHOGENIC MECHANISM

Coronaviruses are single-stranded RNA viruses with a diameter of 60–140 nm. There are four types: α- coronavirus, β-coronavirus, δ-coronavirus and γcoronavirus . Prior to SARS-CoV-2, sixcoronaviruses were known to cause disease in humans, including SARS-CoV and MERS- CoV. SARS-CoV-2, like SARS-CoV and MERS-CoV, is a β-coronavirus . The genome sequence homology of SARS-CoV-2 and SARS is approximately 79%; SARS-CoV-2 is closer to the SARS-like bat coronaviruses (MG772933) than SARS-CoV, which descended from SARS-like bat coronaviruses. Interestingly, several analyses have shown that SARS-CoV-2 uses angiotension- converting enzyme 2 (ACE2) as its receptor, in common with SARSCoV . This virus has the tendency to perceive their analogous receptor over the target cells, due to presence of S proteins on their outer surface and entry inside the cell finallyleads to infection. A structure model analysis shows that SARS-CoV-2 binds to ACE2 with more than 10-fold higher affinity than SARS-CoV, at a level above the threshold required for virus infection.[9]

SOURCE OF INFECTION AND TRANSMISSION ROUTES

Currently, the major source of infection is patients which are already affected with COVID-19 and some patients who are asymptomatic could become carrier of infection, close approximate contact and respiratory droplets are the major spreading route & specific awareness should be given to family members and asymptomatic carriers. Recently SARSCOV-2 has been recognized in the air in ICU, so a long-term vulnerability in comparatively sealed ICU surroundings may result in aerosol communication. Additionally, SARS-CoV-2 has also been detected in the gastrointestinal tract, urine, saliva, and tears of patients with COVID-19[8].

DIAGNOSIS

Diagnosis of corona virus and acquiescence with any of the underlying, could be diagnosed as critical COVID-19 patient. Respiratory anguish in which the rate of respiration is equal or more than 30 breathes per minute. Pulse oximetry oxygen saturation at rest should be equal to or less than 93%. Oxygenation index (Pao2/Fio2) should be equal to or less than 300mm/Hg. If imaging test of lungs were done and shows significant progression i.e., more than 50% in lesion that too within 24 – 48 hours. If patient had undergone respiratory failure and there is need for mechanical ventilation. If patient has underwent shock, along with above discussed features along with failures of other organs.[9]

TREATMENT

Antiviral Drugs Till date, there is no as such specific antiviral drugs for covid-19. But a study revealed that some antiviral drugs like remdesivir, lopinavir and ritonavir could be an effective agent in the treatment of covid-19. But their safety and efficacy in the treatment of covid-19 still requires large sample size for clinical validation. They also stated that interferon-a – nebulization, ribavirin, chloroquinine and umifenovir could also be used in SARS-COV-2 treatment. Immune enhancement therapy, one of the pathogenesis of SARS-CoV is caused by a disproportionate immune response. Boosting the body's immunity is a potential candidate protocol for treating SARS patients. Interferons can inhibit viral infection by inducing both innate and adaptive immune response. Synthetic recombinant interferon α has been shown to be effective for the treatment of patients with SARS in clinical trials, the interferon alfacon-1 plus corticosteroids treatment had a shorter time to 50% resolution of lung radiographic abnormalities compared with corticosteroids treatment alone and was associated with reduced disease-associated impaired oxygen saturation.Moreover, thymosin alpha-1 (Ta1) can be an immune booster for patients with SARS, effectively controlling the spread of disease. [10]

Convalescent plasma therapy

When there are no sufficient vaccines or specific drugs, con- valescent plasma therapy could be an effective way to alleviate the course of disease for severely infected patients in a retrospective survey, it was stated that convalescent plasma therapy is very much considered helpful in treating patient with SARS, which results in reducing hospital stays. Therefore, the plasma of patients who have recovered from COVID- 19 could be collected to prepare plasma globulin specific to SARS-CoV-2. However, the safety of plasma globulin products specific to SARS-CoV-2 deserves further consideration.[10]

Auxiliary blood purification treatment

At present, extracorporeal blood purification technology is used in the treatment of patients with severe NCP. According to the latest

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 525-547 www.ijprajournal.com ISSN: 2456-4494

study, ACE2, the key receptor of SARS-CoV-2, is highly expressed in human kidney (nearly 100 times higher than in lung). Kidney might be the main target of attack for SARS-CoV-2. Early continuous blood purification treatment could reduce renal work- load and help to promote the recovery of renal function. The most severe cases of COVID-19 may suffer froma cytokine storm. The imbalance of pro-inflammatory factors and anti-inflammatory factors may cause immune damage. Therefore, blood purification technology could be used to remove inflammatory factors, eliminate cytokine storms, correct electrolyte imbalances and maintain acid–base balance to control patients' capacity load in an effective manner.[10]

PREVENTION

The best way to prevent infection from COVID-19 is to avoid exposure to the virus. The virus spreads mainly from person-to-person through close contact (within about 2 Gaz). When an infected person coughs, sneezes or talks, respiratory droplets are produced. Other people can catch COVID-19' if they breathe in these droplets.

In addition, people may come to be infected if they touch surfaces, such as doorknobs or tables on which infected droplets have landed, and then touch their mouth, nose or eyes. COVID-19 also spreads by asymptomatic people. The basic preventive measures include simple public health measures that are to be followed to reduce the risk of infection with COVID-19. These measures must always be observed by all individuals.[11]

These include:

Physical distancing

- Ensure a physical distance of at least 2 or 6 feet to reduce the spread; and
- Stay away from crowded environments, where physical distancing cannot beensured.

Use of Mask – wearing a mask properly

- Ensure hand hygiene (thorough washing of hands by soap & water or use an alcohol-based sanitizer), is performed before putting on the mask.
- Place the mask carefully, ensuring it covers the mouth and nose, and tie it securely to minimize any gaps between the face and the mask;
- Avoid touching the mask while wearing it. If a used mask is inadvertently touched, use an alcohol-based hand rub or soap and water to clean hands.
- Replace masks as soon as they become damp with a new clean, dry mask;
- Remove the mask using the appropriate technique: do not touch the front of the mask butuntie it from behind or from the straps.
- After removal of the used mask, clean hands either using alcohol-based hand rub or use soap and water (if hands are visibly soiled); and
- Do not re-use single-use masks. Discard after each use and dispose them of in a closed bin immediately upon removal.

Hand Hygiene

The WHO guidelines on hand hygiene in healthcare (2009) suggest that9 hand hygiene is the single most important measure for the prevention of infection. Practice frequent hand washing (for at least 40-60 seconds) even when hands are not visibly dirty and use alcohol-based hand sanitizers (for at least 20 seconds). Use appropriate product and technique.Rub hands for 20–30 seconds, using an alcohol-based hand rub product is preferable, ifhands are not visibly soiled; and wash hands for 40–60 seconds with soap and running water and dry with a single-usetowel, when hands are visibly dirty or contaminated with proteinaceous material.

Respiratory Hygiene

Respiratory hygiene are measures taken by a person to contain respiratory secretions and prevent the transmission of the infection to other persons. Good respiratory hygiene/cough etiquette can reduce the spread of microorganisms into the environment that cause respiratory infections.

The following measures are recommended:

- Cover the nose and mouth when sneezing and/or Coughing with a tissue or your sleeve/inside of your elbow, to stop the spread of virus.
- Perform hand hygiene afterwards with alcohol-based hand rub products or waterand soap if hands are visibly soiled;
- Stay away from others when ill (particularly for health workers to avoid coming to work when ill);
- Avoid introductory shaking hands;
- Avoid close contact with people who exhibit symptoms.[12]

COVID VACCINES

The four COVID -19 vaccines under development are based mainly onmRNA and DNA

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 525-547 www.ijprajournal.com ISSN: 2456-4494

technologies. mRNA induces cells to produce spike proteins which trigger antibody production while Sinovac uses dead viral particle to induce antibody production. According to CDC, four vaccines have already been rolled out COVID-19 mRNA vaccine BNT162b2 (Pfizer), mRNA-1273 vaccine (Moderna), ChAdOx1 nCoV-19 vaccine / AZD1222 (AstraZeneca), and lastly, the China's Sinovac vaccine.

1. COVID-19 mRNA vaccine BNT162b2 (Pfizer) Vaccine

From the trial involving a sample size of 21720, the vaccine candidates, ≥16 years received 30µg of this mRNA vaccine administered in 2 doses 21 days apart. Among the 21720 candidates who received the vaccine, 8 of them exhibited COVID-19 signs at least one week after the second dose of the vaccine. BNT162b2 showed a protection percentage of 95% (95% CI, 90.3
-97.6) with safety issues indicated by temporary pain at the point of injection, fatigue, and headache which wererated as normal local reactions. Less than 1% experienced severe pain at the injection spot. The vaccine is considered safe for the prevention of COVID-19 infection and the antibodies last for 2 months. The vaccine was approved by U.S. Food and Drug Administration (FDA). The reported side effects were mainly tiredness and headache (59% and 52%, respectively).

2. ChAdOx1 nCoV-19 vaccine / AZD1222 (AstraZeneca)

Thisvaccine was tried in South Africa, United Kingdom, and recently in Brazil with participants receiving 5^10 molecules of the vaccine based on research done by. The Clinical trial phase 3 involved a sample size of 23 848 participants. The overall vaccine efficacy was computed as 70.4% (95% CI, 54.8-80.6, 30[0.5%] of 5807 patients). This viral vector vaccine was shown to be efficacious and safe for combating COVID-19 since only 79 patients out of 5807 who received ChAdOx1 vaccine showed COVID-19 symptoms. The antibody last for 6 months upon vaccination. The vaccine was approved by Institutional Biosafety Committee (IBC). The major side effects included fatigue and headache.

3. China's Sinovac vaccine

China's CoronaVac COVID-19 vaccine that was developed by Sinovac has been proven to be harmless and protective after its third phase trials in various countries across the world, a factor that has boosted the publicconfidence regarding its rollout in different parts of the world. According to scholarly results, Sinovac's vaccine is 100 per cent efficient and effective in preventing moderate infections, 77.9% effective in preventing possible mild cases, and poses an overall efficacy of at least 50.4 per cent in Brazil latest final trials. Vaccine experts have indicated that the trial results are good enough for the vaccine to be enrolled for use among the general population. It is estimated that the antibody last for 6 months upon vaccination[12].

ADVERSE EVENTS FOLLOWING IMMUNIZATION (AEFI)

An adverse event following immunization (AEFI) is any untoward clinical occurrence which follows vaccinations and which does not necessarily have a causal relationship with vaccine use. Adverse events following immunization (AEFI) is defined as 'any untoward medical occurrence which follows immunization and which does not necessarily have a causal relation- ship with the use of the vaccine.' The adverse eventmay be any unfavorable or unintended sign, an abnormal laboratory finding, a symptom, ora disease. The setting is of great importance as, along with the vaccines themselves, the process of immunization is also a potential source of adverse events. Vaccines harbor a variety of components, including antigens, stabilizers, adjuvants, antibiotics, preservatives and residual by products from the production process, all of which have the potential to causeAEFIs. AEFI surveillance in India was started in 1985 along with the Universal Immunization Program (UIP), but AEFI reporting is still suboptimal in the private sector.8 The Pharmacovigilance Program of India (PvPI) follows a spontaneous surveillance method and collects all AEFIs irrespective of the health care setting via Adverse Drug reaction Monitoring Centers (AMCs) across the country, and further transmits this information to a national AEFI committee for investigation and communication as required.9,10But spontaneous reporting system might possibly not collect all AEFIs due to factors such as under-reporting, incomplete reports due to lack of time to fill out forms, health care professionals' tendency to report serious events more frequently than other events, lack of denominator data to calculate incidence rates. This study aimed to detect AEFI to all vaccinesadministered to the pediatrics population at the immunization center of a tertiary care hospital, Mysuru, and to identify predictors of AEFI. AEFIs

can be common and minor (like fever, local pain and swelling), severe (like pain and swelling which spreads beyond the nearest joint or high grade fever) and serious AEFIs (conditions requiring hospitalization or leading to death or disability). [16]

AEFI Classification:

1) Vaccine product–related reaction (an AEFI that is caused or precipitated by a vaccine dueto one or more of the inherent properties of the vaccine product).
2) Vaccine quality defect–related reaction (an AEFI that is caused or precipitated by a vaccine that is due to one or more quality defects of the vaccine product including its administration device as provided by the manufacturer).
3) Immunization-related errors.

4) Immunization anxiety–related reactions.

5) Coincidental events WHO, 2019, Considering the World Health Organization (WHO) criteria, several considerations for assessing causality of an AEFI should be always evaluated:
1) Temporal relationship,

2) Alternative explanations,

3) Proof of association,

4) Prior evidence,

5) Population-based evidence, and

6) Biological plausibility. AEFI might be also related to strains/toxoids and/or to other vaccine components, such as: antibiotics (i.e., neomycin), components of the container (i.e., latex), residual proteins of the substrate (i.e., egg), or stabilizers (i.e., gelatine).[17]

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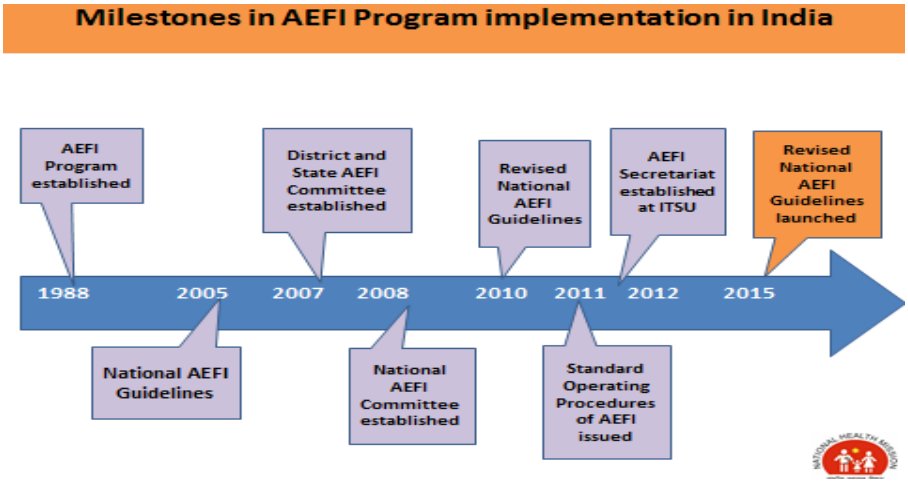

Fig:1.2 Milestones in AEFI program implementation in India

The AEFI Surveillance guidelines are an update to the AEFI Operational Guidelines, 2010 and are in line with the revised WHO/Council for International Organisations of Medical Sciences (CIOMS) guidelines. The key issues covered are:

- Strategies and systems for ensuring quality and safety of vaccines in the country
- Objectives of immunization safety and AEFI surveillance
- New classification of AEFI
- AEFI surveillance system - reporting, investigation, causality assessment and response processes
- Optimum use of vaccine surveillance safety data
- Communication strategy on immunization safety for public andmedia.

Types of AEFIs by severity and frequency:

1. Common minor AEFIs
2. Severe AEFIs
3. Serious AEFIs

Common minor AEFIs: A vaccine induces immunity by causing the recipients immune system to react to the vaccine. Therefore, local reaction, fever and systemic symptoms can result as part of the immune response. In addition, some of the vaccine's components (e.g., adjuvant, stabilizers or preservatives) can lead to reactions.

Severe AEFIs and serious AEFIs: An AEFI will be considered serious if it results in death, requires hospitalization, results in persistent or significant disability/ incapacity or a cluster (two or more cases) of AEFIs occur in a geographical area. AEFIs that are not minor but do not result in death, hospitalization or disability are categorized as severe. „Severe" is used to describe the intensity of a specific event (as in mild, moderate or severe). The event itself, however, may be of relatively minor medical significance**.**

Reporting

The reporting of serious/severe AEFI is done using Case Reporting Format (CRF)(formerly First Information Report), which is prepared by the Medical Officer of the PHC or the reporter and then sent to the District Immunization Officer within 24 hours of getting the information of the case. In the next 24 hours, the DIO verifies the case details and sends it simultaneously to the state and national level. The CRF gives only the most basic details of the affected person, vaccines and session details and status at the time of filling the format.

The other channel of reporting serious and minor AEFI from the level of occurrence of the AEFI up to the national level is through monthly progress reports. This is done using existingmonthly immunization reporting formats such as the ones for National Rural Health Mission (NRHM), Health Management Information system (HMIS) etc.

It is necessary for the peripheral health staff to submit a NIL monthly report in case no AEFI is detected from their area during the month. Minor AEFI that are brought to the notice of the health staff as a concern should be reported and documented in a line list.[18]

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 525-547 www.ijprajournal.com ISSN: 2456-4494

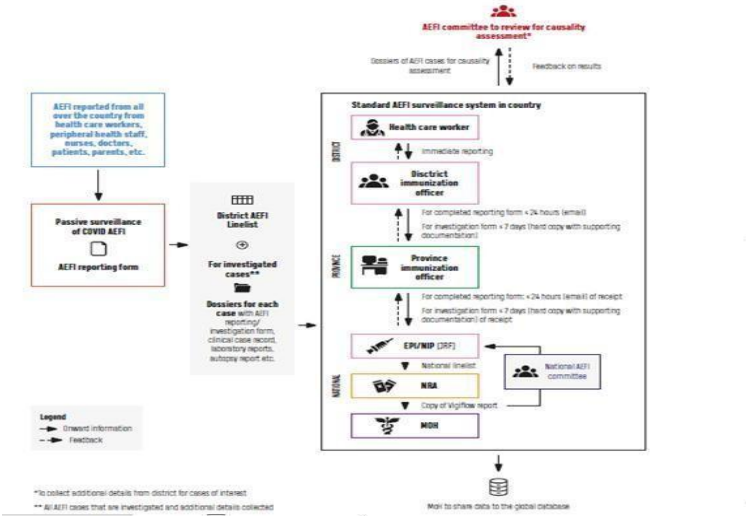

Fig :1.3 AEFI Investigation including lab sample collection

Investigation of reported sudden unexplained deaths following vaccination

Investigationof unexplained deaths following immunization is an issue of great importance with regard to the immunization programme. Proper causality assessment would enable differentiation of vaccine related deaths from deaths due to other causes. A special document has been developed to improve investigation of unexplained AEFI deaths. The verbal autopsy form hasbeen designed based on the WHO and Centers for Disease Control and Prevention (CDC) sudden infant death investigation (SUIDI) form, whereas the guidance on conducting autopsyhas been developed by a committee of leading experts in the field of immunology. The format should be filled by the investigating team while investigating the reports of AEFI deaths where information regarding the event is inadequate, such as

- Brought dead to health facility,
- Home death,
- Insufficient medical records regarding the event,
- Death in case that was not hospitalized or

The guidelines give the guidance for conducting autopsy in cases of reported deaths. An autopsy must ideally be performed in every case of an AEFI death within 72 hours of deathby forensic specialist or medical officer.

Causality Assessment

Causality Assessment is the systematic evaluation of the information obtained about an AEFI to determine the likelihood of the event having been caused by the vaccine/s received. It is a critical part of AEFI monitoring and enhances confidence in the national immunization programme. The revised guidelines use the new revised WHO/CIOMS Causality (2014).

The Guidelines encourages the state to conduct Causality Assessment for reported AEFI cases. The AEFI report must have investigation formats, relevant documents and a diagnosis for being eligible for Causality Assessment. [19]

The Causality Assessment process has four steps:

1. ***Eligibility***: To determine if the reported AEFI case satisfies the minimum criteria for Causality Assessment as mentioned above.
2. ***Checklist***: To systematically review the relevant and available information to address possible causal aspects of the AEFI
3. ***Algorithm***: To obtain a direction as to the Causality with the information gathered in the checklist.
4. ***Classification***: To categorize the AEFI"s association to the vaccine/vaccination based on direction determined in the algorithm.

All the cases being investigated by the district should be assessed by the causality assessment experts of the state AEFI committee after discussing all the investigation formats and reports available. It is recommended to disseminate the results so that others can learn from the experience. Immunization errors will need to be corrected and for coincidental incidents, communication to maintain confidence is necessary.

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 525-547 www.ijprajournal.com ISSN: 2456-4494

AEFI Committees

The revised guidelines also give the detailed information on the AEFI Committees (district/state/ national) along with the terms of reference of the committee members. AEFI Committees provide technical inputs to review the factors leading to the adverse event and provide inputs to improve the system to provide safe and effective immunization. The committee should include members from various departments like pediatrician, microbiologist, pathologist, epidemiologist, neurologist, forensic expert, cold chain officer, representatives from IDSP, drug authority, and municipal corporation and partner agencies. [20]

Monitoring of AEFI surveillance

The guideline emphasizes on monitoring performance of the AEFI Surveillance system. The key indicators defined are as follows:

For routine AEFI:

1. Percent of routine reports (zero reports) received on time
2. Percent of AEFI cases line listed
3. Percent of Serious AEFI cases

For serious AEFI:

1. Percent of Serious AEFI cases reported on time
2. Percent serious AEFI cases with Case Reporting Form (CRF) shared with the state and centre on time
3. Percent of Serious AEFI cases investigated on time
4. Percent of Serious AEFI cases with completed investigation
5. Percent of Serious AEFI cases classified for causality by the state AEFI Committee on time

Vaccine risk communication and handling of media

Effective communication around vaccine safety including management of public reactions requires serious investment of resources and efforts towards strategic communication for Immunization. The guidelines introduced the strategic communication plan to address the short-term crisis(in cases of AEFI) and long-term support that the immunization programme require at the national and local level. The plan focuses on regular communication with the community and local media on RI activities to encourage use of vaccines and thus help in improving the vaccine coverage levels. An AEFI response protocol has standardized procedures for communication to help handle a crisis promptly and in the correct manner. It identifies the spokesperson who will respond in crisis situations at all the levels. The protocol recommends that in case of media interest in anAEFI crisis, a press release should be issued as early as possible (preferably within first 6 hours).

National Regulatory Authority and its affiliated institutions and convergence with AEFI Surveillance Program:

The guideline describes the role of National Drug Regulatory Authority and Pharmacovigilance Program of India PVPI and the importance of coordination between the CDSCO and the Immunization Division, MOHFW. The results of the causality assessment approved by the National AEFI Committee is shared with the CDSCO which analyses the results to take further necessary regulatory actions (such as inspections, amendments to product inserts, reporting by manufacturers, etc.). The IPC (Indian Pharmacopoeia Commission) has established a data sharing arrangement with the AEFI Secretariat for ensuring convergence in vaccine safety reports and their adequate investigations.[20]

Causality assessment of potential COVID-19 vaccine-related AEFIs

Table :1.1 Causality term Assessment criteria	
Certain	Event or laboratory test abnormality, with plausible time relationship todrug intake • Cannot be explained by disease or other drugs • Response to withdrawal plausible(pharmacologically, pathologically) • Event definitive pharmacologically or phenomenologically (i.e., anobjective and specific medical disorder or a recognized pharmacological phenomenon)

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 525-547 www.ijprajournal.com ISSN: 2456-4494

	• Rechallenge satisfactory, if necessary
Probable / Likely	• Event or laboratory test abnormality, with reasonable timerelationship t drug intake • Unlikely to be attributed to disease or other drugs • Response to withdrawal clinically reasonable • Rechallenge not required
Possible	• Event or laboratory test abnormality, with reasonable timerelationship intake • Could also be explained by disease or other drugs • Information on drug withdrawal may be lacking or unclear
Unlikely	• Event or laboratory test abnormality, with a time to drug intakethat Makes a relationship improbable (but not impossible) • Disease or other drugs provide plausible explanations
Conditional / Unclassified	• Event or laboratory test abnormality • More data for proper assessment needed, or • Additional data under examination
Unassessable / Unclassifiable	• Report suggesting an adverse reaction • Cannot be judged because information is insufficient or contradictory Data cannot be supplemented or verified

Tools for AEFI

It is recommended to use the existing data collection tools, as described in the Global Manual on Surveillance of AEFI for data collection, collation and processing for AEFIs. Some of the tools need to be amended and adapted to the context of the COVID-19vaccine safety. The details of some available and how to access them are provided in Table1 .

Table 1.2: Tools recommended for COVID-19 vaccine-related AEFI reporting, investigation, management and causality assessments

Description	Purpose	Status for COVID-19	Electronic tool
AEFI reporting form	To collect basic reports of all AEFI cases that have been notified	COVID-19 standard AEFI reporting form that includes the nameof the manufacturer and brand name	Use in-country tools if available; if not WHO recommends Vigiflow
AEFI linelist	To collate the details in the reporting form	COVID-19 standard linelist that includes the name of the manufacturer and brand name	WHO recommends Vigiflow
AEFI investigation form	To collect detailed information when serious AEFI cases are investigated	Adapted to include COVID-19 specific questions	WHO AEFI investigation assistance software

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 525-547 www.ijprajournal.com ISSN: 2456-4494

AEFI causality assessment (available here)	To determine case classification of serious AEFI cases	Remains unchanged	Global Vaccine Safety on-linecausality assessment tool

II. LITERATURE REVIEW

1. Michel halim *et.al* (2009) evaluated that journal of clinical and medical research and its workout about vaccine, types of vaccine, and doses of vaccine.

2. Mangala kumari jeyanathan *et.al* (2009) evaluated that immunological condition for COVID-19 vaccine strategic its workout about the vaccine, routeof vaccine, and types of vaccine and clinical trials of vaccinated candidates.

3. Jeetu *et.al* (2010) evaluated that pharmacovigulance: A world-wide master key for drug safety monitoring that work out about, the current global networkof pharmacovigilance centre and drug safety issues beyond the boundaries andit also explains about the pharmacovigilance centre and their roles in future.

4. Sanvidhan G Suke *et.al* (2015) evaluated that role of pharmacovigilance in India, and here we explain about the discovery of the interaction amongst the drugs and their effects in humans

5. Viccolo lambardi *et.al* (2019) evaluated that vaccine safety in children and in general population in a pharmaceutical study on AEFI anti identity vaccine in Italy. It was studied about the study performance on suspected AEFI reports for children and adults who receive any form of vaccination and it can be seen here according to their ratios that depend upon the effects that they faced.

6. Juny Sebastian *et.al* (2019) evaluated that active surveillance of adverse events following immunisation (AEFI) a prospective 3-years vaccine given to the children and for those adverse effects.

7. Dr.Abhishek sharma *et.al* (2020)evaluated that journal of current medical research and opinion and here wehave seen about the detailed knowledge about the covid-19.

8. Dr.Abhishek sharma *et.al* (2020) evaluated that journal of current medical research and opinion and here we have seen about the detailed knowledge about effects occur after the vaccine given to the children.

9. Prachi Rai, Vansh jatana *et.al* (2019) evaluated that survey on COVID-19 vaccination in India and here it workout about the use of vaccine, side effects, and it also explains about the the covid-19.

10. Shobha Rani *et.al* (2021) evaluated that Indian journal of pharmacy practice (IJOPP) the official journal of association of pharmaceutical teachers of India (APTI) workout about research articles, review articles and case reports in thediverse area of pharmacy practice like clinical pharmacy, hospital pharmacy, and community pharmacy.

11. Karen fong *et.al* 2021 evaluated that rapid diagnostic tests modern-day tools in the realm of infectious diseases and it explains about role of bacteria, fungi and viruses during the infectious time and here we can see the full knowledge behind the disease related bacteria.

12. Christy Cecil forehand *et.al* 2021 evaluated that productivity tracking: A survey of critical care pharmacist practise and satisfaction and it workout about critical care pharmacy describes two tiers of responsibilities: 1) essential 2) desirable activities where those categorised into five domains.

13. Ann Barrett et.al 2021 evaluated that mapping the literature of hospitalpharmacy workout about the study desires the literature of hospital pharmacy and identifies the journals most commonly cited by authors in the field. The study also looks like different citation practices between journals with a wide audience compared to a national journal with a focus on regional issues that trend in the field.

14. Olaf Rose et.al 2021 evaluated that enhancing medication therapy in the Parkinson's disease by establishing an interprofessional network including pharmacists here it explains about primary, secondary and territory carefacilities across professionals.

III. AIM AND OBJECTIVES

Aim:

To conduct a Prospective Observational Study on Pharmacosurveillance on Covid vaccines Adverse Effects Following Immunization (AEFI).

Objectives:

1. To analyze Age Group Distribution of Adverse Drug Reactions on Covid Patients
2. To analyze on Gender wise vaccination rate.
3. To find out the Age wise causality Assessment on Covid Patients

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 525-547 www.ijprajournal.com ISSN: 2456-4494

4. To find out Overall Causality Assessment of ADRs on Covid Patients.
5. To demonstrate the gender Wise Causality Assessment on Covid Patients
6. To analyze Gender wise Causality Assessment on each Covid Vaccine
7. To find out the Social History of Covid Patients
8. To find out Previous Medical History of Covid Patients

IV. METHODOLOGY

The study was designed by the department of pharmacy, Narasaraopet Institute of Pharmaceutical Sciences at Narasaraopet. After getting approval from authentic research authorities of the institution the study was conducted. The study was conducted by keeping patient details off the records. This was a study conducted on adverse effects following immunization (AEFI) on corona virus vaccines viz COVISHIELD & COVAXIN respectively.

STUD DYESIGN: A Prospective Observational Study**.**

STUDY SITE: At both online and offline platforms i.e., in google platform through google sheets as well as in college in AEFI form collected in various places of Narasaraopet, Guntur district**.**

STUDY PERIOD: Six months**. SAMPLE SIZE:** 300

STUDY CRITERIA:

INCLUSION CRITERIA:

- Patients who have been vaccinated either single shot or both shots successfully.
- Patients of all age group was included in the study
- Patients of both genders was included in the study

EXCLUSSION CRITERIA:

- Patients who are uninterested to participation in the study was not included.
- Patients who had not been vaccinates with covid vaccines were not included in the study.

SOURCES OF DATA:

- Collecting data's from directly interacting participants through AEFI forms both online and offline

PROCEDURE

As given, after receiving prior approval from authentic research authorities of our institution, the study plan was put to execution by prioritizing the confidentiality of the patient personal information. AEFI survey was conducted at the college surrounding as well as at the online platform and then study details were collected for a time period of 6 months.From these AEFIs were estimated thoroughly in the study. Each AEFI sheet contains patient information particulates such as name, age, sex, address, contact information, post medication history i.e., prior to vaccination, social history, past medication history i.e., a prolonged therapy pertaining to a disease, name of vaccine administered, date of vaccination both 1st and 2nd doses individually and their adverse effects respectively.

Patients were given unlimited time and multi response option so they could fill the form carefully and as many responses as needed in case though online. Because not all forms were fully completed, we also conducted offline surveys in our college premises as well as in our neighborhoods.

The seriousness of reactions was evaluated according to WHO Criteria. ADRs were analyzed for causality using WHO causality assessment. The collected data were recorded in Excel sheet using a structure format containing importantly age group, past medication history, social history, post medication history, name of vaccine, ADRs 1st and 2nd dosing, other significant effects and comment section. Then lastly the acquired data was interpreted statistically.

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 509-524 www.ijprajournal.com ISSN: 2456-4494

V. RESULTS

From the 300 cases collected 169 Adverse Drug Reactions were identified and included for the analysis.

Table: 5.1. Age Group Distribution of Adverse Drug Reactions on Covid Patients

Age Interval	No. of ADRs	Percentage (%)
18-45Years	72	43
+45Years	97	57

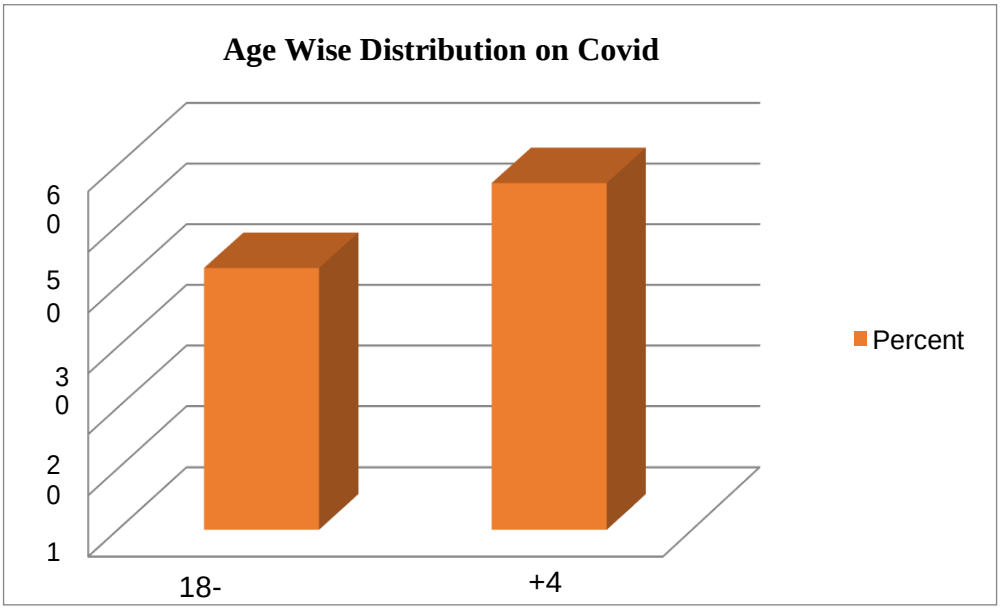

Fig: 5.1. Age Wise Distribution on Covid Vaccine

Table: 5.2. Gender wise Distribution of Adverse Drug Reactions on Covid Patients

Gender	No of ADRs	Percentage (%)
Male	80	47
Female	89	53

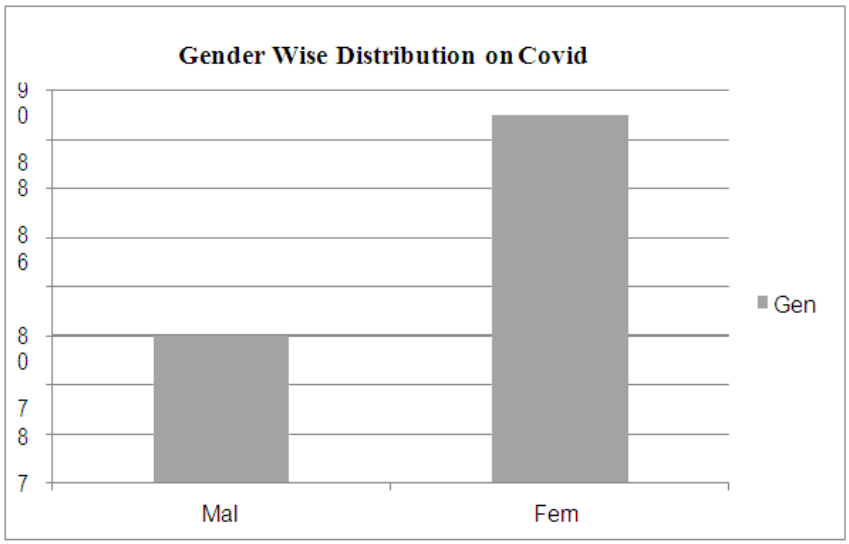

Fig:5.2. Gender Wise Distribution on Covid Patients

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 509-524 www.ijprajournal.com ISSN: 2456-4494

Table: 5.3 Age wise causality Assessment on Covid Patients

Age Group	No. of ADRs	Percentage (%)
18-45Years	72	43
+45years	97	57

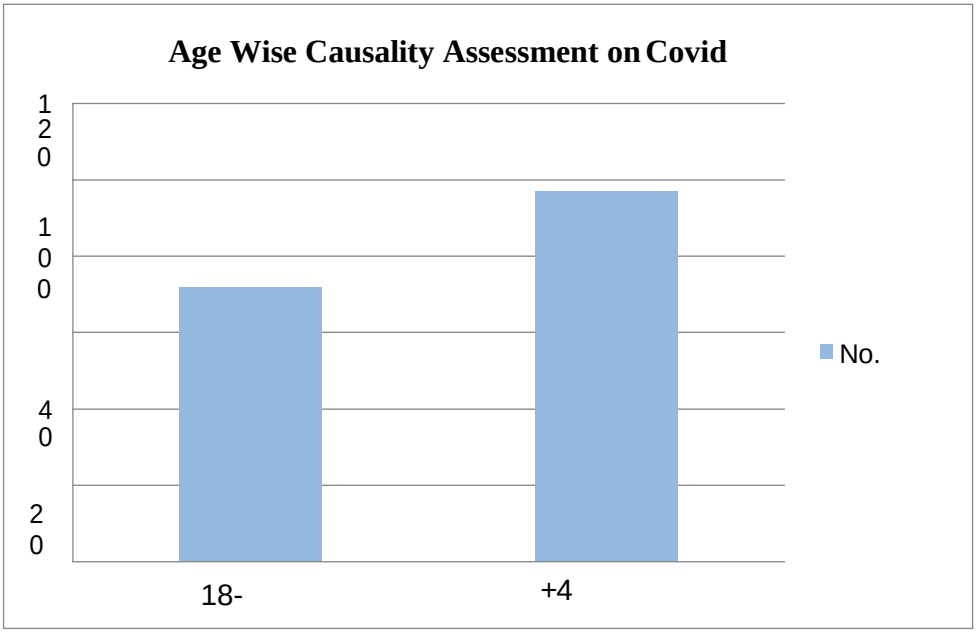

Fig: 5.3. Age wise Causality Assessment on Covid Patients

Table: 5.4. Overall Causality Assessment of ADRs on Covid Patients

Type of ADR	No of ADR	(%) of ADR
Definite	6	3
Probable	76	45
Possible	76	45
Doubtful	12	7

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 509-524 www.ijprajournal.com ISSN: 2456-4494

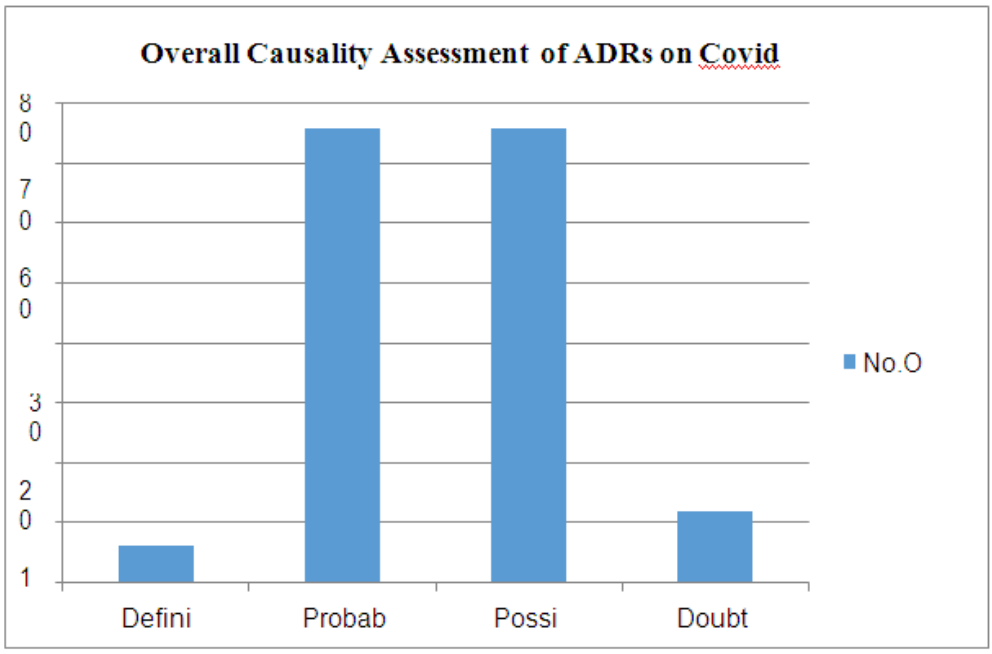

Fig:5.4. Overall Causality Assessment of ADRs on Covid Patients

Table: 5.5 Gender Wise Causality Assessment on Covid Patients

	Causality				Total No of ADRs	Percentage (%)
	Definite	Probable	Possible	Doubtful		
Male	4	38	37	6	85	51
Female	2	38	38	6	84	49

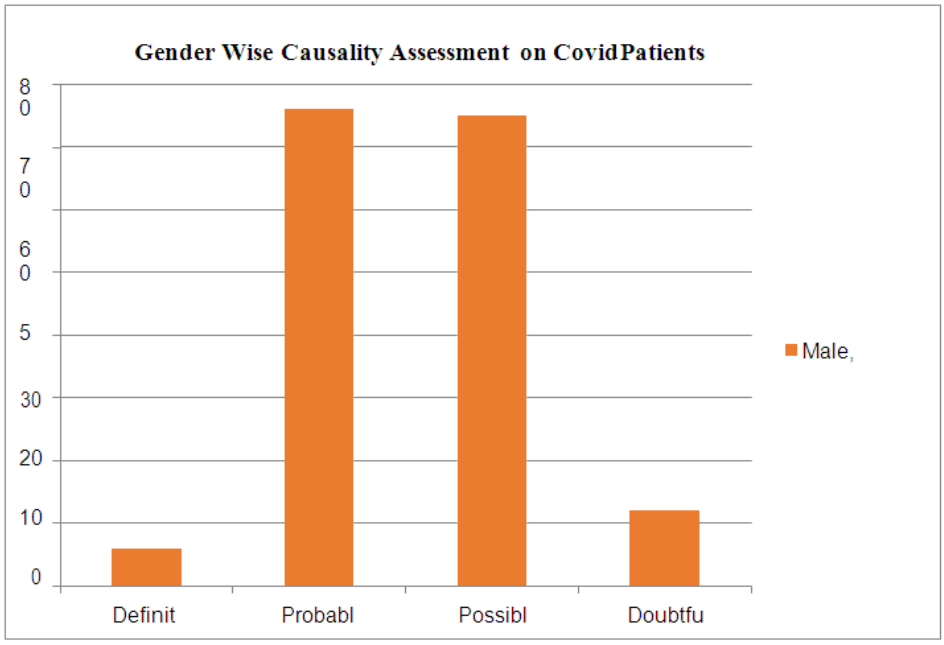

Fig :5.5. Gender Wise Causality Assessment on Covid Patients

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 509-524 www.ijprajournal.com ISSN: 2456-4494

Table :5.6. Gender wise Causality Assessment on each Covid Vaccine

Drug	Causality	Gender	
		Male	Female
Covaxin	Definite	-	-
	Probable	5	8
	Possible	6	6
	Doubtful	3	-
Covishield	Definite	1	1
	Probable	30	30
	Possible	31	31
	Doubtful	-	3
Others	Definite	1	-
	Probable	3	-
	Possible	-	-
	Doubtful	-	-

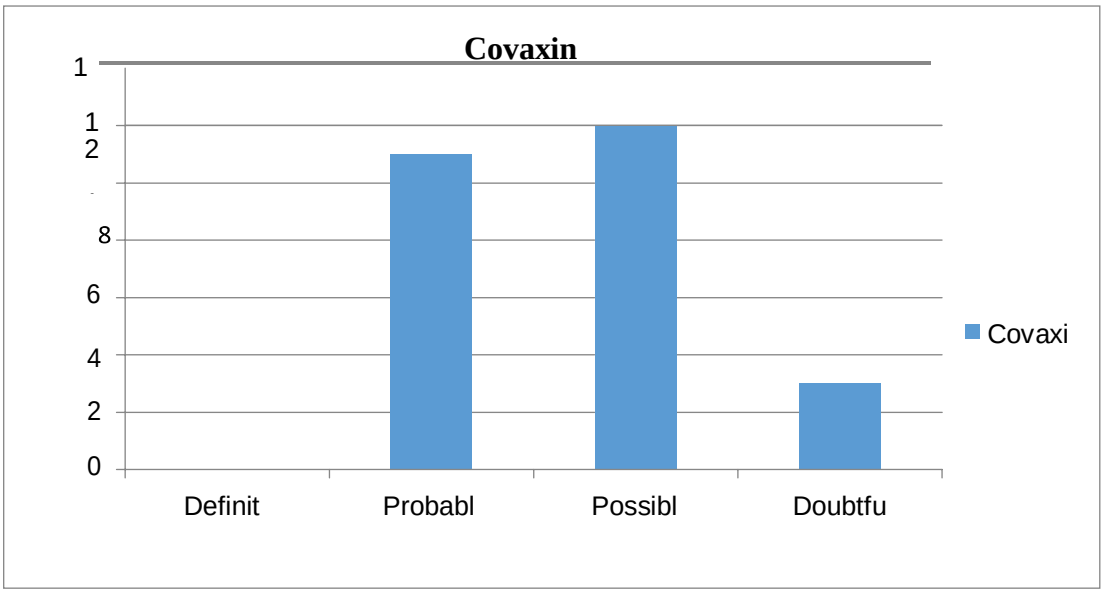

Fig :5.6.1. Gender wise causality Assessment on Covaxin Vaccine

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 509-524 www.ijprajournal.com ISSN: 2456-4494

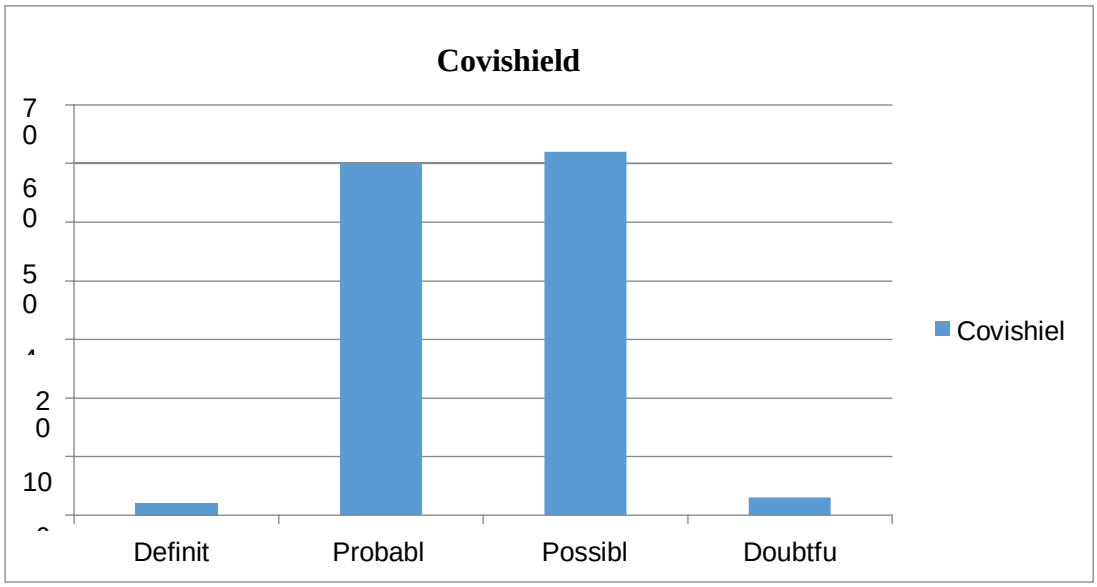

Fig :5.6.2 Gender wise Causality Assessment on Covishield Vaccine

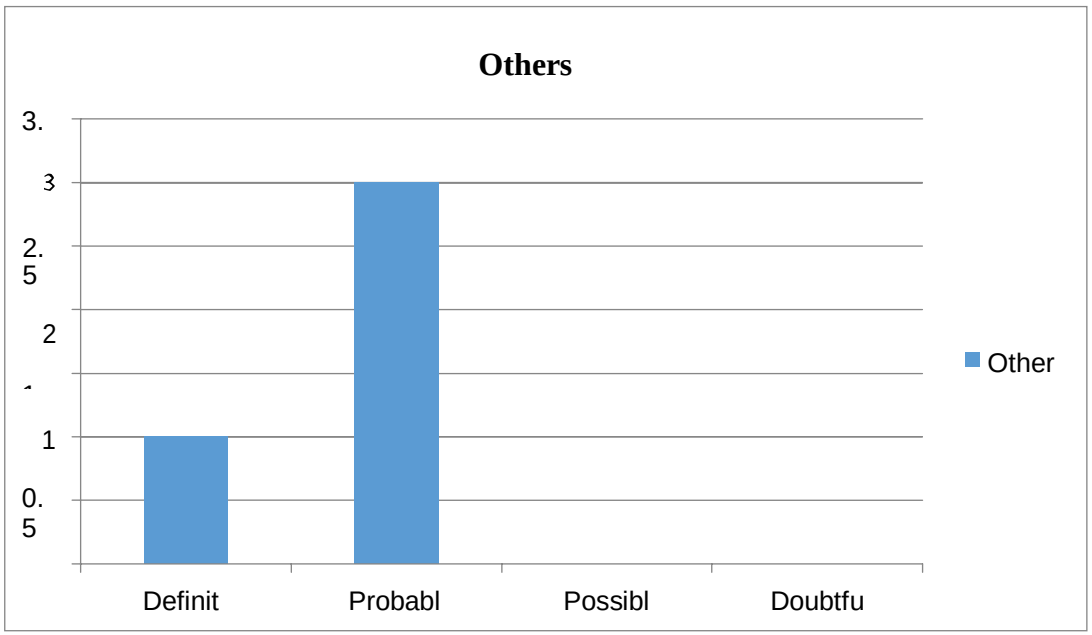

Fig :5.6.3 Gender wise Causality Assessment on Other Vaccines

Table :5.7. Social History of Covid Patients

Social History	No. of Covid Patients	Percentage (%)
Smoking	8	2.7
Alcohol	8	2.7
Not Applicable	286	95.3

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 509-524 www.ijprajournal.com ISSN: 2456-4494

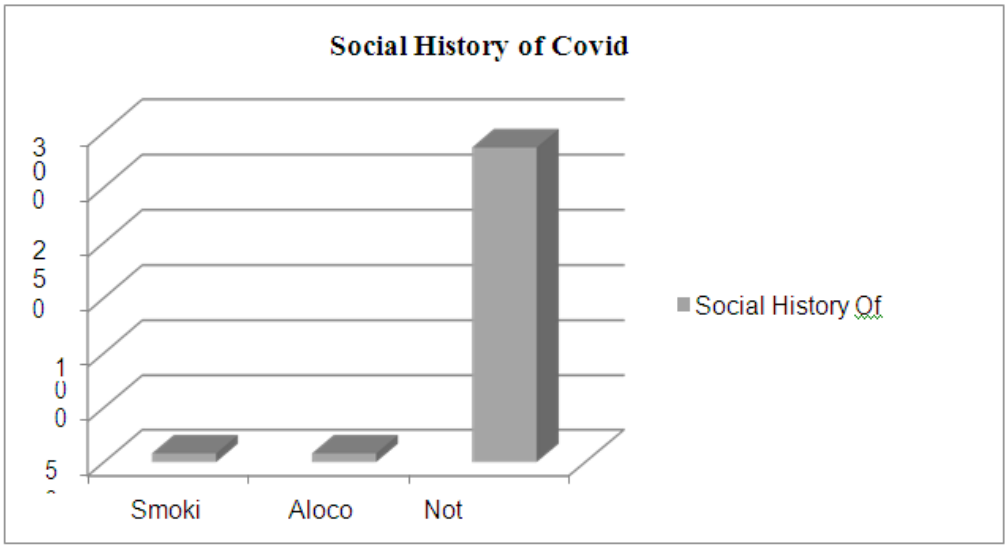

Fig: 5.7. Social History of Covid Patients

Table :5.8 Previous Medical History of Covid Patients

Previous Medical History	No. Of Covid Patients	Percentage
Diabetes	14	4.7
Hypertension	15	5
Kidney Problem	2	0.7
Liver Problem	0	0
Heart Problem	2	0.7
Others	52	17.3
Not Applicable	223	74.3

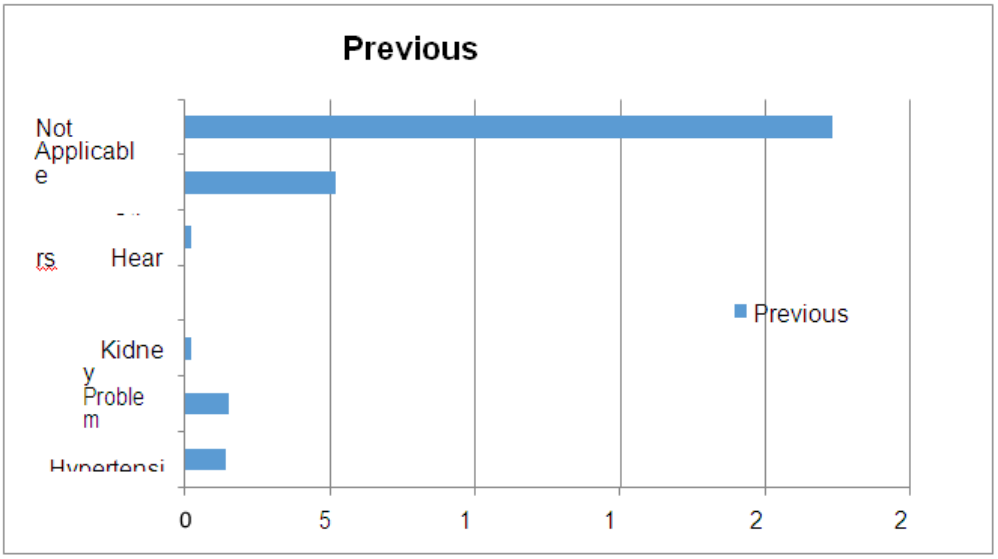

Fig :5.8. Previous Medical History of Covid Patients

international Journal of Pharmaceutical research and Applications
Volume 6, Issue 6, pp: 509-524 www.ijprajournal.com ISSN: 2456-4494

VI. DISCUSSION

A Prospective observational study on adverse event following immunization (AEFI) on COVID vaccines viz., Covaxin and Covishield was conducted by online and offline mode in Narasaraopet, Guntur district for the period of 6 months and a total of 300 cases were included in protocol. Also, an inform consent form in local language were designed and collected from patients during the study. The study demographic data showed a moderately equal incidence of ADRs in both male and female subjects.

Out of the 300 total cases, 169 ADRs were detected and reported to the ADR monitoring center, guntur using adverse events following immunization reporting forms (AEFI). The Data includes age, gender, ADR, severity of the event, dosage, frequency, and route of administration etc.

Most found ADRs in our study **fever, headache, body pains, pain at injection site, redness at injection site** (>100), These ADR's were already reported. Fever, Headache, Body pains, Pain at Injection Site, Redness at Injection Site by the Covishield, Covaxin and Others Vaccines by the definite, probable, possible, doubtful ADRs found in our study.[15]

The seriousness of the reactions was analyzed by using WHO Causality Assessment scale. Causality assessment proved fever occurred with 7.2 %, body pains occurred with 24.2 %, headache occurred with 4.6 %, pain at injection site occurred with 16.3 %, redness atinjection site occurred with 1.3 %.

Out of the total ADRs found 3%were definite, 45% were probable and 45% were possible, and 7%were doubtful and 47% were found in males and 53% were found in females. And 4% definite ADRs in females and 2% definite ADRs in males 38% probable ADRs in males,38% probable ADRs in females, 37% possible ADRs in females and 38%possible ADRs in males, and 6%doubtful ADRs in females and 6%doubtful ADRs in males.[16]

According to gender wise causality assessment for each vaccine shows Covishield in males were 62 and in females were 66. Covaxin in males were 14 and in females were 14, other vaccine in males were 4 and in females were 0. Overall males and females show equal ratioin ADR's.[17]

The causality assessment shows that 169 reported ADRs were, definite, probable, possible, and doubtful. The restricting to the framework of the study interventions were not madeand re-challenge was not done due to ethical reasons.

VII. CONCLUSION

A successful ADR surveillance can have a positive impact on the medication use system to improve the quality of patient care and in reducing the occurrence of ADR. Pharmacist has a very important role in monitoring and reporting of ADR. We perform our study for the monitoring and reporting of ADRs for COVID vaccines through online and offline mode at Narasaraopet, Guntur District for a period of 6 months and we detected 169 ADRs out of 300 cases.

Among them males show 47%% ADR's whereas females show 53% ADR's. Most found ADRs in our study fever, headache, body pains, pain at injection site, redness at injection site**,** by Covishield, Covaxin, and the other vaccines were definite probable, possible, and doubtful ADRs found in our study.

This study helps the Indian Pharmacopoeia Commission (IPC) in detecting, monitoring, and reducing the percentage of occurring ADRs thereby providing safety for the patient community. **Also, we conclude the two vaccines namely Covaxin & Covishield were safe with mild side effects, which can be manageable.**

Limitation of study:

- The time duration 6 months not sufficient for giving confirmatoryreport.
- The sample size should be done in greater number for betterresult.
- Some of the ADR reported are previously reported.

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