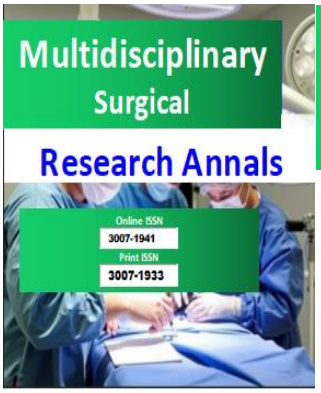

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The Study and Management of the Prevalence and Control Measures for the Foot and Mouth Disease Virus (FMDV)

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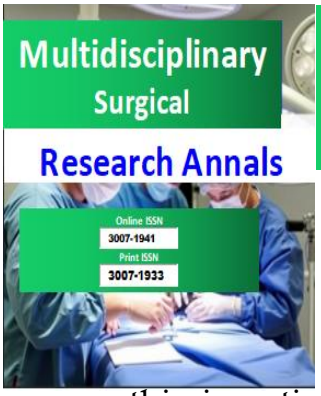
Abstract

Introduction: The Foot-and-mouth disease (FMD) virus is an extremely contagious pathogen that presents a significant danger to livestock. Its capacity to generate chronic illness and long-term repercussions on various animal species highlights the pressing need to comprehend its epidemiology and institute effective control measures. In Pakistan, the prevalent FMD serotypes are O, Asia-I, and A. **Purpose:** The purpose of



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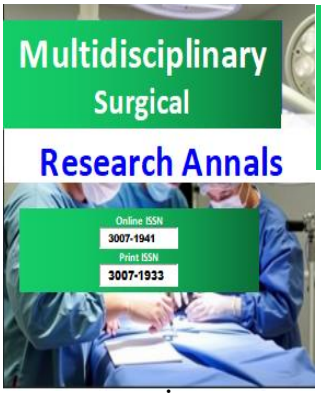
this investigation was to explore the prevalence of FMD in different districts of Punjab, with Sheikhupura district displaying the highest prevalence (54%) and Chakwal district the lowest (10%). **Methodology:** The investigation utilized a blend of microbiological and veterinary methodologies. Viral isolates were gathered from infected animals and subjected to serotyping and genetic characterization to identify the precise FMD virus serotypes and strains circulating in the region. The RNA genome of the FMD virus, a single-stranded positive-sense RNA virus, was evaluated using molecular techniques. The presence of the viral capsid, which encloses the 8.3-kb genome, was confirmed through capsid protein analysis. To manage the spread of FMD, vaccination strategies were executed. The efficacy of varied vaccine formulations and their ability to prompt protective immune responses were assessed. The investigation aimed to enhance the potency of the vaccines to broaden the range of protection against diverse FMD serotypes. The materials utilized in this research comprised FMD viral isolates, serotyping reagents, molecular biology tools, and various vaccine formulations. **Results:** The results demonstrated the importance of migration and interactions between vulnerable and infected animals as



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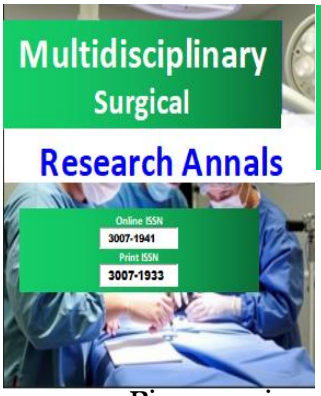
primary routes of FMD virus transmission. The presence of multiple serotypes and various host species, including wildlife, presented significant challenges to disease management. **Conclusion:** However, the findings highlighted the potential of vaccines in eradicating the virus and safeguarding animals from FMD. The research outcomes contribute to the understanding of FMD epidemiology and provide valuable insights for the development of improved control strategies.

Keywords: Foot and mouth disease, Serotypes, IRES, hoofed animals, CFT

Introduction

Foot-and-mouth disease virus is known as the most infective illness and most probably it attacks on cattle, sheep's, goat, cows etc. and for the cattle business in many nations it play role as a supplier for a very long time (Li et al., 2021). More than 120 years after its discovery, the FMDV is still a major cattle microbe, with annual expenses from productivity failures and immunization approximately US$6.5–US$21 billion in endemic areas of FMDV (Poonsuk et al., 2018). The contributing factor to the financially most significant wildlife illness, foot-and-mouth disease virus, is an icosahedral symmetric non-enveloped aphthovirus that is a member of the picornaviridae family (Rowlands, 2008).



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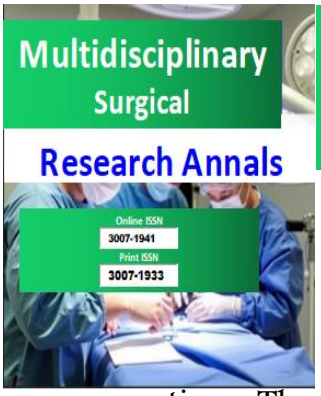
Picornaviruses have a positive-sense RNA genome with only one strand that is generally between 7,200 and 8,500 nucleotides long and encased in a non-enveloped capsid that is around 30 nm in diameter (Logan et al., 2018) . The viral genetic code is a positive-sense RNA genome with only one strand having lengthy 5′ untranslated region, a short 3′ UTR and a big open reading frame (ORF), measuring around 8.3 kb in length. VP1, VP2, VP3, and VP4 are four structural proteins that make up the 8 non-structural proteins (Lpro, 2A, 2B, 2C, 3A, 3B, and 3Cpro) and icosahedral capsid that control virus assembly, RNA replication and protein folding (Logan et al., 2018). FMDV is brought by seven immunologically unique serotypes of the species FMD virus: A, O, C, Asia 1, South African Territories (SAT) 1, Asia 1, SAT 2, and SAT 3 (Aphthovirus genus, Picornaviridae family)) (Nick J Knowles et al., 2007) A, O, and C types were discovered in South America, Europe, the northern half of Africa and Asia, however their distribution is expanding. 3 kinds of SAT were discovered for the very first time in Southern Africa, however their species are expanding throughout Africa, with South African Territories 1 making an appearance in the Middle East. From far east to the eastern Mediterranean, Asia 1 is found in Asian



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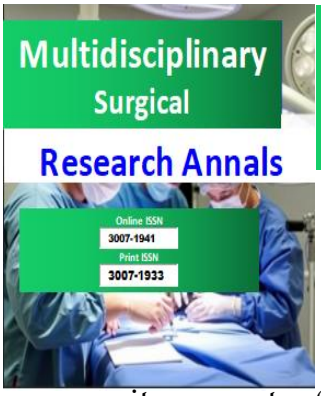
nations. The inability to cross-react after infection by separate kinds first distinguished these types, however the introduction of lab techniques allowed for fast discovery of distinctions inside and among types (sub-type strains). Competition hybridization was used to compare the RNAs of the 7 serotypes of the FMD Virus. The three European serotypes (A, O, C) as well as the Asia 1 serotype, shared 60 to 70% homology. The three serotypes from Southern African Territories (SAT 1, SAT 2, SAT 3) had similar homologies, nonetheless, there was little commonality between the two groups substantially bottom 25 to 40 percent. Within serotypes A and O, there was more similarity between the RNAs of different subtypes (Robson et al., 1977).

Weakness, temperature and tubular sores on mouth foot and teats are all signs of FMD (Alexandersen et al., 2003). FMDV has a wide host range, with 70 or more species vulnerable, including cattle, sheep, pigs, goats, and buffaloes (Grubman & Baxt, 2004a; Jamal & Belsham, 2013). FMDV is hypothesized to be transferred mostly via aerosol droplets between animals in close proximity. FMD has a big impression on cattle sector and poses a danger to worldwide animal and animal product commerce. As a result, the Office International des Epizooties has classed



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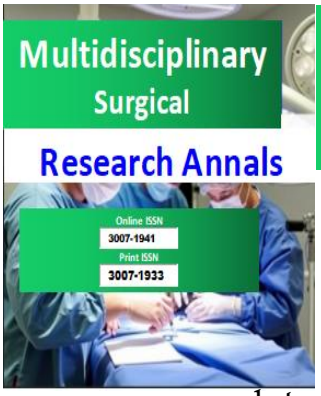
it as part of the A list of animal infectious illnesses (Knight-Jones & Rushton, 2013; Perry & Rich, 2007).

Although mature animals usually recover, the morbidity rate in naive populations is relatively high, and several species experience substantial pain and misery. Although FMD has a low fatality rate, it reduces cattle production and prevents afflicted nations from participating in international animal and animal product commerce. Unfortunately, FMD is enzootic in many undeveloped parts of Asia, Africa, and South America, limiting economic progress(Rowlands, 2008). The European epidemic of FMD in 2001/2002, which mostly afflicted the United Kingdom, is expected to cost 6000 million Euros. (Samuel & Knowles, 2001).

Epidemiological Analyses of Foot and Mouth Disease in Pakistan

The most common serotypes in Pakistan are O (70 percent), Asia-I (25 percent), and A (4.67 percent), which cost farmers Rs. 6.00 billion each year. Due to cost, long land boundaries, and the lack of a regional programmed covering the entire region rather than a single country, an elimination policy (stamping out) cannot be persuaded in most regions of the world, including Pakistan. As a result, vaccination is the only



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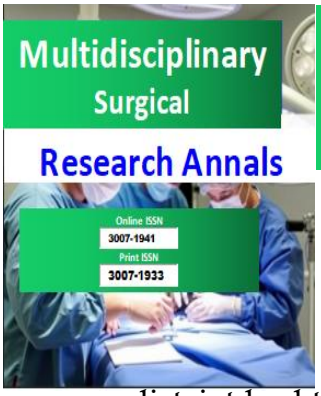
approach to control the disease in Pakistan at the moment.

The highest prevalence (54%) was found in Sheikhupura district, while the lowest (10%) was found in Chakwal district in Punjab. Khanewal district had the most importance (33 percent), while Bahawal Nagar district had the lowest (0.5 percent). In Sindh, Sanghar district had the highest prevalence (33.78 percent), while Ghotki district had the lowest (12.09 percent). Karachi district had the highest importance (36.20 percent), while Ghotki district had the lowest (10.04 percent).In the NWFP, Kohat district had the highest prevalence (37.33 percent), while Swat district had the lowest (19.35 percent). Haripur district had the highest importance (20.75 percent), while Manshera district had the lowest (9.4%).

The highest prevalence (70 percent) was found in Chagi district, while the lowest (2.50 percent) was found in Gawader district in Balochistan. Lasbella district had the highest importance (3.55 percent), while Turbat district had the lowest (0.5 percent). Mirpur district in Azad Jammu and Kashmir (AJK) had the highest prevalence (30.65 percent), while Palandri district had the lowest (6.64 percent). Mirpur district had the most importance (12.77 percent), while Rawala Kot



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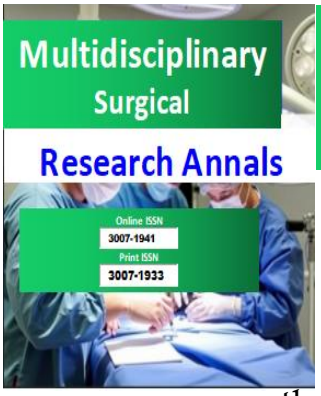
district had the lowest (7.11 percent).

FMD was listed as the most prevalent ailment in the Islamabad Capital Territory (ICT), with a prevalence of 25.5 percent and a prevalence of 19.2 percent.

Transmission

Despite the massive amounts of the FMD virus discharged a look at the surroundings and the severe sensitivity of the host species to infection, FMDV transmission is not always predicted. In endemic areas, viral propagation frequently uses both direct and indirect animal contact; nonetheless, limited occurrences like fomite and wind-borne aerosol could serve as seeds for incursions into FMD-free nations(David J. Paton et al., 2018).

The migration and the interaction between susceptible animals and diseased animals are two most typical ways for the FMD virus to spread. Every excretion and secretion shed a virus, including the breath of infected first phase of the disease in animals sickness. Peak viral production occurs when clinical indications develop in cattle and pigs, but before lesions appear in sheep, and then it rapidly drops in all species as antibody generation and some other immune reactions



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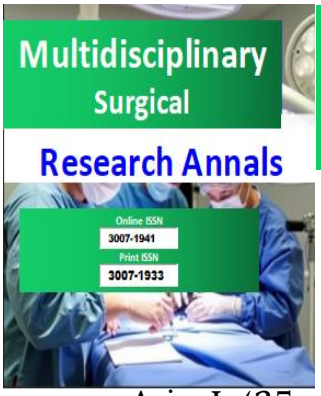
suppress the infection. In contact animals can be infected by virus through aerosol or oral routes, as well as cutaneous abrasions, which is most common in pigs(R. P. Kitching, 2005).

People, automobiles, surgical equipment, brushes and other fomites can mechanically spread the FMD infection of vulnerable animals with a virus. In Denmark in 1982 and Italy in 1993, doctors were engaged in the outbreak of FMD, with the latter practicing artificial insemination while on a contaminated farm, and the former performing surgery on contaminated surgical equipment. Accordingly, farmers were blamed for the virus's spread among sheep flocks during the 2001 outbreak. However, as with the 136 R.P. Kitching infected animal items, infection requires close contact between the susceptible animal and the polluted fomite(R. P. Kitching, 2005).

FMDV is non-enveloped aphthovirus that belongs to Picornaviridae family. This cattle microbe causes the annual loss of approximately US$6.5–US$21 billion in FMDV endemic areas. FMDV is brought by seven immunologically unique serotypes of the species FMD virus: A, O, C, Asia 1, South African Territories (SAT) 1, Asia 1, SAT 2, and SAT 3. The most common serotypes in Pakistan are O (70 percent),



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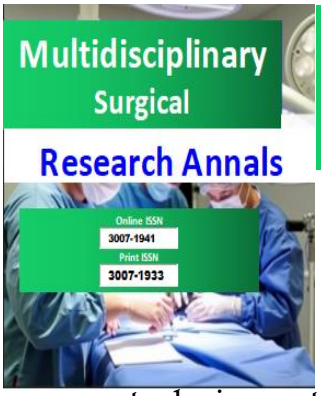
Asia-I (25 percent), and A (4.67 percent), which cost farmers 6.00 billion rupees each year. Vaccines developed against are effective for only small period of time (4–6 months).

Material and Methodology

The current study utilized a range of microbiological and veterinary techniques to examine the prevalence, serotypes, genetic traits, and transmission patterns of Foot-and-mouth disease (FMD) virus. Additionally, different vaccination strategies were assessed to enhance the effectiveness and widen the protection of vaccines against diverse FMD serotypes. The objective of this research was to contribute to the knowledge of FMD epidemiology and offer guidance for the development of improved control strategies.

Sample Collection: Samples of viral isolates were obtained from affected animals in various districts of Punjab, Pakistan. Animals with clinical signs of FMD such as weakness, temperature, and tubular sores on mouth, foot, and teats were the source of these samples.

Serotyping and Genetic Characterization: The viral isolates collected were analyzed through serotyping and genetic characterization



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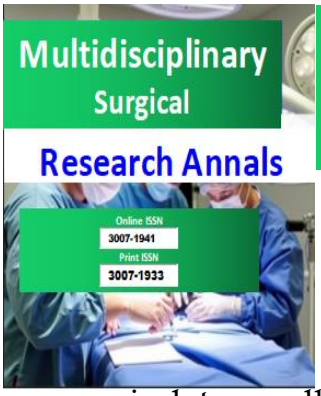
techniques to identify the specific serotypes and strains of FMD virus prevailing in the region. The serotypes were identified using serotyping reagents, while genetic characterization involved molecular biology techniques.

RNA Genome Evaluation: The RNA genome of the single-stranded positive-sense RNA FMD virus underwent evaluation using molecular techniques. The genome was examined to determine its length, structure, and genetic composition.

Capsid Protein Analysis: Capsid protein analysis confirmed the presence of the viral capsid, which encloses the 8.3-kb genome. This analysis included studying the structural proteins (VP1, VP2, VP3, and VP4) and their role in virus assembly, RNA replication, and protein folding.

Vaccination Strategies: Different vaccination strategies were implemented to control the spread of FMD. Various vaccine formulations were assessed for their effectiveness and ability to induce protective immune responses in animals. The aim was to enhance the potency of the vaccines and broaden their protection against diverse FMD serotypes.

Study Materials: The materials used in this research included FMD viral



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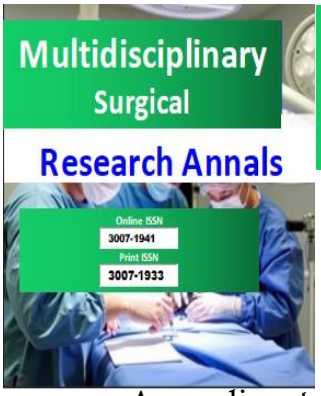
isolates collected from infected animals, serotyping reagents for identifying serotypes, molecular biology tools for genetic characterization, and various vaccine formulations for evaluating their efficacy.

Prevalence Assessment: The prevalence of FMD in different districts of Punjab was determined by calculating the percentage of infected animals in each district. The prevalence rates were calculated based on the number of infected animals divided by the total number of animals sampled in each district.

Transmission Analysis: The transmission of FMD virus was analyzed to comprehend the routes of spread. The role of migration and interactions between vulnerable and infected animals as primary routes of transmission was investigated. Factors such as aerosol droplets, direct and indirect animal contact, and fomite transmission were taken into account.

Results

The goal of this work was to use previously experiments that have been published to calculate the ratio of transmission of foot & mouth disease virus from infected animals to vulnerable nonhuman organisms.



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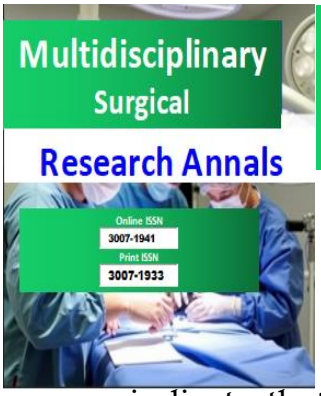
According to our findings, a carrier infects 0.026 animals every month on average. Furthermore, the percentage of animals that is positive declines by 0.11 every month during the carrier era. These two variables can be used in risk assessment models that are constructed quantitatively. When FMDV is infected in cattle acutely, the frequency at which FMDV spread from infected animals to vulnerable ones is far lesser than the ratio predicted (Tenzin et al., 2008).

Only African Buffaloes to cattle and impalas have been found to transmit Field FMDV transmission from carrier species to hosts at risk situations (Aepyceros melampus). Moreover, infection has been brought on by injecting carrier animal saliva into cattle and pigs in experimental conditions, while there is no evidence on whether this may happen in the field or with species that are closely related to it, such Asian buffaloes(Klein, 2009). The Foot and Mouth Disease Virus (FMDV), belonging to the Aphthovirus genus in the Picornaviridae family, presents significant challenges for vaccine development due to its high genetic diversity. Current vaccines, comprising chemically inactivated whole viral formulations, struggle to provide effective cross-protection against various FMDV serotypes (D. J. Paton et al., 2005). Studies



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indicate that vaccines targeting specific serotypes demonstrate higher efficacy compared to those targeting multiple strains (Black et al., 1986; Lyons et al., 2017). Efforts to control FMDV through vaccination face hurdles such as the need for large-scale virus production, stringent containment facilities, and the requirement for frequent updates to match circulating virus strains (Sobrino et al., 2001). Moreover, vaccine-induced immunity typically wanes after 4–6 months, necessitating regular booster shots to maintain protective levels (Parida, 2009). Despite vaccination, a considerable proportion of vaccinated animals may still carry the virus in their pharyngeal epithelium, indicating potential gaps in vaccine efficacy (P. Kitching et al., 2007).

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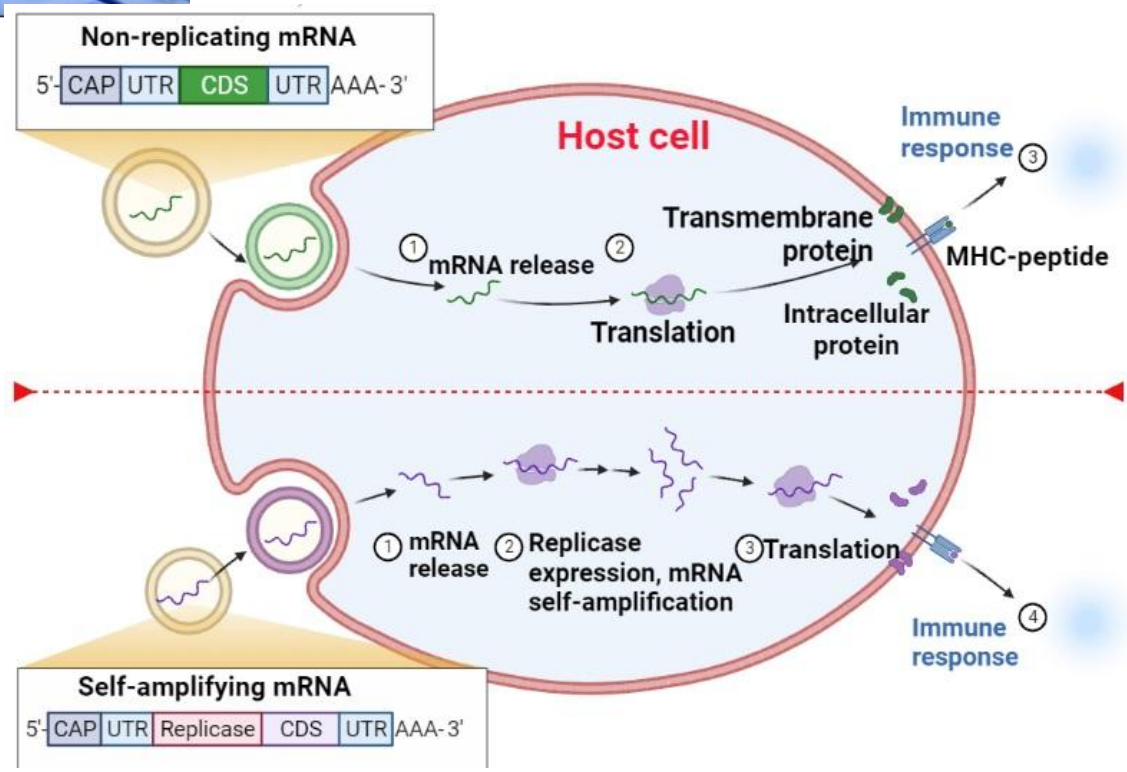
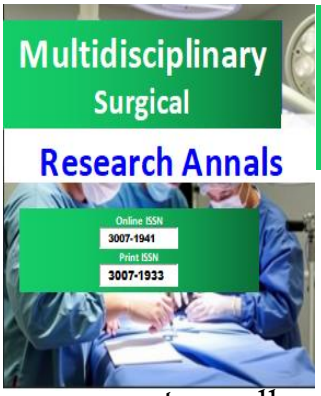


Pic: biorender.com

Pic 3.1: The immunological expression of foot and mouth virus, its way of transmission.

In Vivo Vaccine Matching

An in vivo cross-protection test is the direct comparative matching test in which animals after vaccination are confronted with the virus. While vaccination and exposure of animals to outbreak virus are highly successful in assessing protection, they are time consuming, costly, and need considerable infrastructure, including the supply of suitable biosecurity protocols and practices, which are not always available. So



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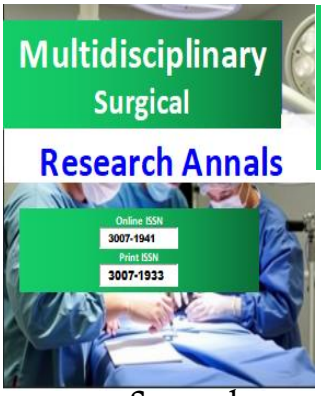
yet, small number of researches has been attempted to directly check this comparative matching test. In 2008, Brehm with his colleagues directed numerous heterologous protection experiments with serotype A of foot and mouth disease virus, and the in vitro r1-value in all of them indicated that the vaccination virus was not a good match (Brehm et al., 2008).

In Vitro Vaccine Matching

Serologically, several indirect vaccination matching (in vitro) assays are available. These investigations examine the reactivity of a BVS raised against the vaccine strain to be tested with the relevant field virus. In Foot and Mouth Disease, three serological approaches are used to evaluate candidate vaccination strains for cross-protective vaccine strain selection: I two-dimensional viral neutralization test (2D-VNT), (ii) liquid phase blocking enzyme linked immunosorbent assay (LPBE), and (iii) complement fixation tests (CFT). For each reference BVS, a one-way indirect antigenic connection value ("r1-value") is calculated using in vitro vaccine matching. To perform these matching tests of vaccine, field isolates must be serotyped and modified to cell culture growth conditions in order to achieve viral titers for serological evaluation.



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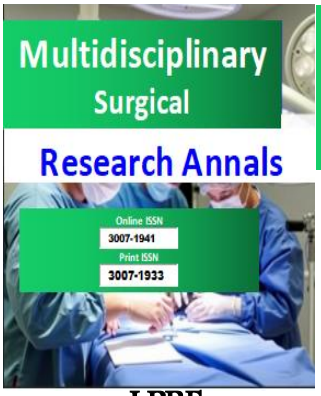
Several aspects like different cell lines used in different and poor viral growth in cell culture can greatly affect conclusions. The evaluation of FMD vaccines involves rigorous testing methods. In vivo cross-protection tests, though resource-intensive, provide valuable insights into vaccine efficacy (Brehm et al., 2008). In vitro assays such as the Virus Neutralization Test (VNT), Liquid Phase Blocking Enzyme-Linked Immunosorbent Assay (LPBE), and Complement Fixation Test (CFT) offer alternative approaches for assessing vaccine strains' cross-protection (M. M. Rweyemamu et al., 1978). Each assay has its advantages and limitations in predicting vaccine efficacy. Understanding the molecular mechanisms of FMDV replication and host immune responses is crucial for vaccine development and disease control. Key viral proteins such as RNA polymerase (3D), proteinase (Lpro), and structural proteins (e.g., VPg, 2B, 2C) play essential roles in viral replication and assembly (Grubman & Baxt, 2004a). The host immune response involves complex interactions between viral proteins and host cellular machinery, with viral proteins modulating host immune pathways to facilitate viral replication (Cottam et al., 2006).



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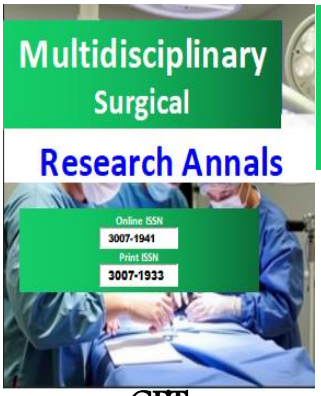
LPBE

Blocking the Liquid Phase Enzyme-Linked Immunosorbent Assay identify any leftover pathogen following an interaction between diluted serum as well as a pretreated viral dosage overnight solution (Kitching et al., 1988) and is utilized for vaccine matching in various FMD standard labs. This examination has a great significance over VNT in that it is faster and needs smaller amounts of sera after vaccination, which are sometimes scarce (Mana Mahapatra & Parida, 2018).

In most cases, there is no clear differentiation between the VNT and LPBE readings (R. P. Kitching et al., 1988). There are however, some discrepancies in between the results of two sets which is likely due to the fact that the viral protein in the neutralizing assay must have the ability to avoid neutralization of serum and reproduce in cells, whereas the LPBE simply assesses antibody binding to immobilized antigen. It's difficult to say which approach delivers the better indication of host protection when the VNT and ELISA procedures don't give the same results, though neutralization of active viral proteins should be characterized as more accurate predictor for neutralization of serum(Mana Mahapatra & Parida, 2018).



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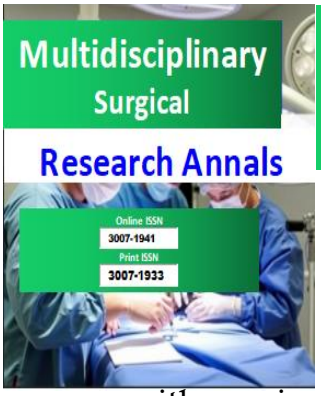
CFT

CFT, like LPBE, uses a antiserum of guinea-pig developed against the strain of vaccine to determine the connection between the strain of vaccine and the field isolate. This test is presently mostly used in South American countries, however It has recently been used significantly less. This test is commonly used as a diagnostic instrument. The most reliable assays for FMD virus vaccine matching are currently the VNT and LPBE, but they are not usually repeatable. As a result, without completing several experimental duplicates, it is extremely impossible to evaluate the tests or have entire assurance in the outcomes. Furthermore, both assays (VNT and LPBE) have the problem of not exactly reflecting what will occur in vivo.

In ruminants, conventional aqueous vaccines produce protective immunity 8–10 days after initial immunization, a subsequent shot is necessary to keep the immune system at a protective level for about six months. Following that, depending on the epidemiological circumstances, more regular booster shots are necessary to keep immune responses protective (Cox et al., 2003). The extent of the response will unavoidably be influenced by variation between serotypes



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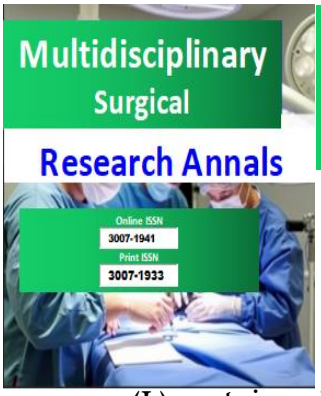
with varying levels of immunogenicity. Because only the sheep got a one vaccine shot, these findings imply the need for more potent emergency vaccinations, particularly oil adjuvated formulations, compared to standard aqueous vaccines, may have benefits.

Translation and Replication of FMD Virus

Picornaviruses are the RNA viruses that are icosahedral, unenveloped, and are a member of the positive-strand RNA virus. There are currently 68 genera and 158 species in the family Picornaviridae, which contains variety of well-known human and other creatures infections (Zell et al., 2021). The Picornaviridae family's genome is made up of an Positive monoisotopic single-stranded RNA that is contagious (Racaniello & Baltimore, 1981)n, except for Dicipivirus genus, or Cadicivirus A, which has an anisotropic DNA (Reuter et al., 2018). The picornavirus gene encoding a polyprotein, which virally encoded proteases process through proteolysis into 11-15 mature proteins by the polyprotein precursors are cleaved in a series of primary and secondary cleavages, depending on the species (Willem, 2016).

AUG1 and AUG2, two in-frame evolutionary conserved starting codons are present in FMDV RNA and are exploited culminating in the leader



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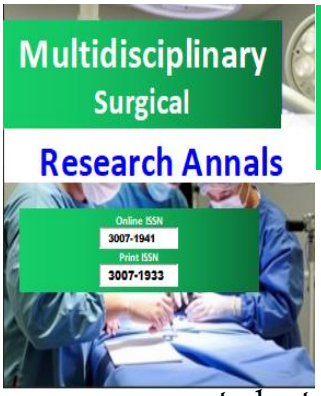
(L)proteins Lab and Lb, respectively, as sites of protein synthesis beginning. (G. J. Belsham, 1992).

In contrast to most Picornaviruses, Dicipiviruses have intergenic region (IGR) that separates both structural and nonstructural proteins have coding regions. (Reuter et al., 2018). In this regard, in a study conducted, the (Ras-related protein Rab1b, a Golgi brefeldin A-resistant GBF1 regulatory molecule, and the small GTPase ADP-ribosylation factor Arf5 proteins) were all implicated and all play a role in the FMDV IRES-containing RNA localization at the ER-Golgi junction (Fernandez-Chamorro et al., 2019a). Picornavirusesco-opt several host RNA-binding proteins like (RBPs) that aid in RNAs from viruses are drawn in for viral protein metabolism as well as construction comparable to several other RNA viruses, has complexes that control viral RNA production. (Walsh & Mohr, 2011). The ability of viral IRES components to function outside of their normal background of RNA promotes cap-independent process in a variety of inherited situations. In fact, this characteristic have been used to produce artificial proteins bicistronicity structures in a variety of situations shortly after their discovery (Encarnación Martínez-Salas, 1999). The IRES of FMDV is



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expected to possess complicated secondary structure comparable to those of EMCV IRES (E. V. Pilipenko et al., 1989). The genomic RNA of FMDV is approximately 8.3 kb in length (G. J. Belsham, 2005). The replication of genetic material is an important part of any virus's lifetime. As a result of exquisite in vitro investigations, several of the molecular features of replication have been thoroughly established. It has been established that a number of viruses can replicate in macromolecular assemblies that include both viral and cellular constituents (Bienz et al., 1983; Gosert et al., 2003; Knox et al., 2005; Monaghan et al., 2004; Novoa et al., 2005; Schlegel et al., 1996).

The structure of the picornavirus 3Dpol, like that of other DNA and RNA polymerases, looks like a right hand cupped, with three distinct subdomains called (thumb, fingers, and palm) (Brautigam & Steitz, 1998; Steltz, 1998). The replication structure is shown in Picture 3.2.

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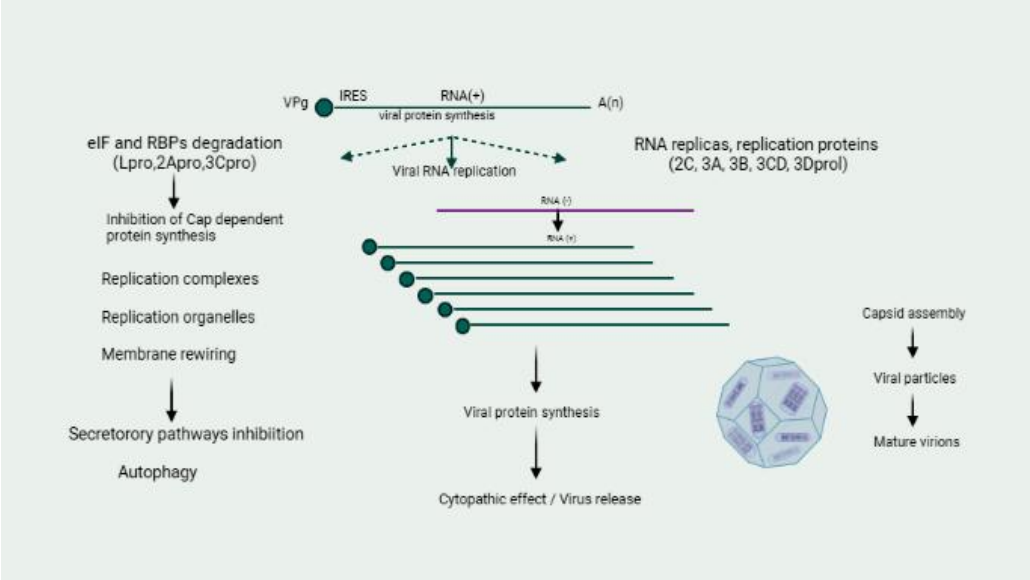
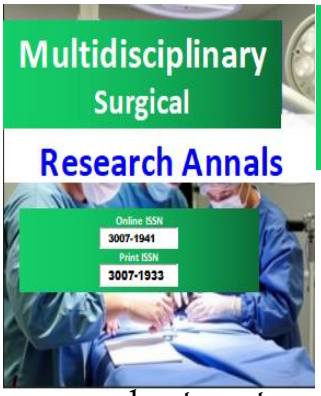


*Pic: biorender.com

Pic 3.2 The figure shows the replication of FMD virus. Replication proteins (2C, 3A, 3B, 3CD and 3Dprol) are involved in the replication process that synthesize viral proteins. These viral proteins release viruses. Mature virions are formed by the capsid assembly.

Immune Response of Host to FMDV

Positive sense single stranded RNA genome is found in FMD virus. FMDV belongs to family Picornaviridae family of Aphthovirus genera (Grubman & Baxt, 2004b).Transcription in host and cap dependent translation is switch off by FMDV and replicate efficiently in the host. Animals that are infected by FMDV, the virus starts replication at the infection site in the respiratory system. The initial line of defense of the



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host system that is innate immune system suppresses by virus. RNA genome of FMDV is translated into polyprotein as a ORF (open reading frame). Viral encoded proteolytic enzymes primarily convert the polyprotein into mature viral particles. FMD Virus codes for ten NS (Non-Structural) proteins and 4 VS (Viral Structure) proteins. Along this, a number of precursor proteins yield by proteolytic cleavages.

2A, 3C, Leader (L), an 18 amino acid peptide having proteinase action and are NS proteins. These proteins take part in viral polyprotein processing (Graham J. Belsham et al., 2000). Non-Structure proteins take part virus replication process. 3D is an RNA polymerase that is dependent on viral RNA. VPg is known as 3B that is bound to 5' end of RNA of virus through covalent bond. It plays an important role in synthesis of RNA by initiation. There is requirement of replication of viral RNA and capsid assemblage that is membrane sequence which is fulfilled by 2B, 2C and 3A proteins (Grubman & Baxt, 2004a) . Recent work indicates that some precursors and NS proteins are involved in regulating the response of the host(Cottam et al., 2006). Lpro is a proteinase that resembles papain. In the host, Lpro shutting down cap dependent translation of mRNA.by cleaving eIF4G initiation factor.

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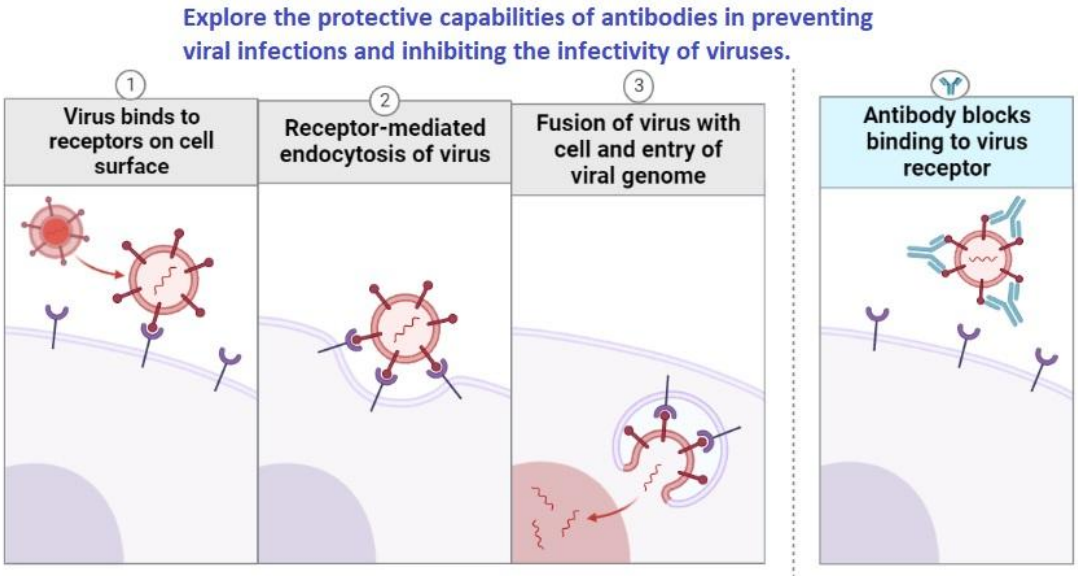
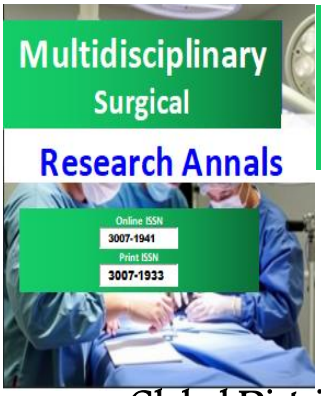
Therapy with IFN-α/β, suppresses the replication of FMDV and showed that stimulated genes, protein Kinase which is RNA dependent and RNase L are reported to be associated in inhibition process. By inhibiting host mRNA translation, especially IFN-/ mRNAs, Lpro limits the response of innate immunity to viral illness in primary cells and susceptible animals. In IFN capable cells, the lack of Lpro in leaderless virus causes a shortened phenotype (de los Santos et al., 2006). The immunological mechanism is shown in picture 3.3.



•Pic: biorender.com

Pic 3.3: The antibiotics expression while viral attack.



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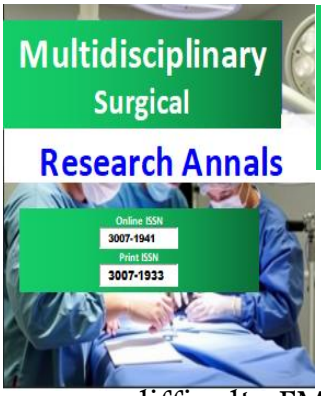
Global Distribution of FMDV

The threat of introducing this virus into imported animals as well as their products hinders commerce in these products from infected regions. Diseases caused by this virus can be managed, but several obstacles should be overcome, such as the presence of many serotypes of the causal virus and a variety of host species, including wildlife. FMDV is one of the most contagious illnesses in animals and was first discovered as a cause of animal disease (Brito et al., 2017). Although FMD causes low mortality in infected animals, epidemics have major economic repercussions because of nonstop damages such as reduced milk and meat production, treatment costs, and trade restrictions on animals as well as on animal products (James & Rushton, 2002; Nampanya et al., 2012; Perry et al., 2002; Perry & Rich, 2007) and a high level of contagiousness (Abubakar et al., 2012).

Serotype A

There are more than thirty variants of serotype A of foot and mouth disease virus, which is biologically and antigenically more variable among all the serotypes. As it is the most antigenically and genetically variable serotype, vaccine regulation of FMD Serotype A is extremely



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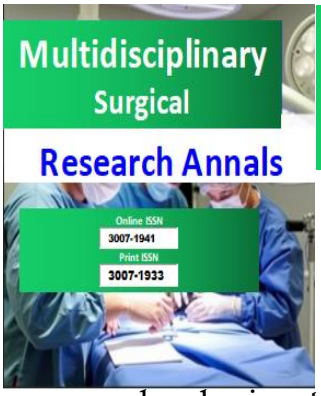
difficult. FMDV serotype A is thought to have originated in South America, according on sequence research. In 2011, outbreaks of Serotype Were indeed recorded in Afghanistan, Turkey, India, Bhutan, Malaysia, and Yemen, as well as Myanmar in 2010.(Abubakar et al., 2012).

Serotype O

Serotype O of FMD is found globally, especially in the Middle East and South Asia. In 2000–2006, Foot and Mouth Disease virus serotype O Pan-Asian were found in Japan, Korea, Mongolia, Russia, the UK, France, and South Africa (Cottam et al., 2006). During 2009, the O serotype was recorded in China, Thailand, Taiwan, Hong Kong, and Myanmar in Southeast Asia, and in Pakistan in Central Asia. In the Middle East, outbreaks of the O serotype were recorded in Yemen, Egypt, and the United Arab Emirates in 2009.

Serotype C

As compared to other FMDV serotypes, serotype C spreads to a smaller area. In Europe and South America, vaccination had managed foot and mouth disease virus serotype C, and it was eradicated in some countries of Asia and Africa too. Type C was discovered to belong to the



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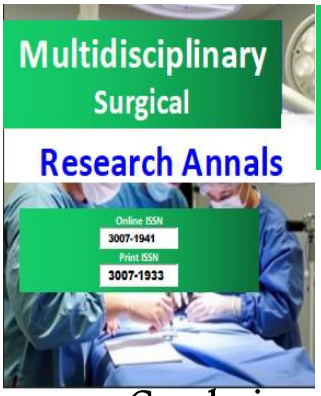
developing topotype Philippines C, which originated in 1970s in South America (M. Rweyemamu et al., 2008). In 1995, a type C virus outbreak was discovered in the eastern area of Pakistan (Jamal et al., 2010).

Serotype Asia 1

This serotype outbreak has been ongoing throughout the Indian subcontinent and nearby countries. Phylogenetic study of the Foot and Mouth Disease virus VP1 gene revealed that the virus belonged to the sixth group within the Asia 1 serotype (Jean Francois Valarcher et al., 2009). In 2004, outbreaks of this serotype were recorded in Kyrgyzstan and Tajikistan, then epidemics in Eastern Russia, Mongolia, and parts of China in 2005–2006 (J. F. Valarcher et al., 2005). In 2011, outbreaks of FMD serotype Asia 1 were reported India, in Turkey, and Afghanistan.

Serotypes SAT

A number of investigations in Southern Africa have established that the African buffalo can carry Foot and Mouth Disease virus serotypes SAT-1, SAT-2, and SAT-3 in their bodies. Egypt reported 20 FMD serotype SAT-2 outbreaks in dairy cattle in various regions in 2012, while twenty-three Foot and Mouth Disease virus serotype O, A, and SAT-2 outbreaks in cattle and buffaloes was reported in Libya.



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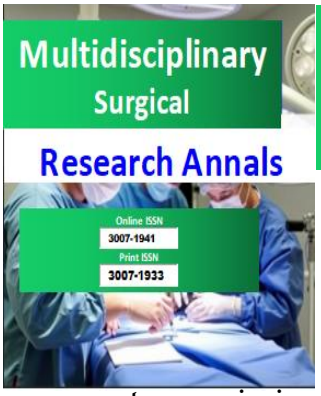
Conclusions And Future Perspectives

This study explains the transmission, translation and replication process and immune response of host to foot and mouth disease virus. FMDV is non-enveloped aphthovirus that belongs to Picornaviridae family. FMDV comprises a positive-sense RNA genome that is single stranded and its length is about 8500 nucleotides long. Numerous vaccines have been developed to protect cattle from FMDV but death rate is still high causing noteworthy economical loss. High mortality rate shows the ineffectiveness of formulated vaccines. New better vaccines should be developed to eradicate this curse from the world. The present investigation aimed to examine the ubiquity of Foot-and-mouth disease (FMD) in various districts of Punjab, Pakistan, and to evaluate the efficiency of vaccination techniques for regulating the disease. The results indicated that FMD is extensively widespread in the area, with diverse degrees of infection throughout the districts. The analysis employed a blend of microbiological and veterinary methodologies to identify the prevalent FMD virus serotypes and strains, as well as to appraise the efficiency of several vaccine formulations. The results highlight the importance of animal migration and interactions in virus



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transmission, and also emphasize the challenges presented by the existence of multiple serotypes and diverse host species. Nonetheless, the study exhibited the potential of vaccines in eradicating the virus and protecting animals from FMD. These insights contribute to a better comprehension of FMD epidemiology and offer valuable knowledge for the advancement of improved control techniques. Additional research and sustained efforts are necessary to refine vaccination approaches and enlarge the spectrum of protection against diverse FMD serotypes. By implementing effective control measures, we can mitigate the impact of FMD on livestock and safeguard animal health and welfare in the region.

Conflict of interest: The authors show no conflict of interest

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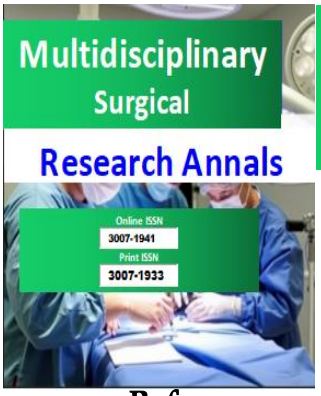
Authors Contribution: Lyba Bashir, Nimra Shehzadi and Arslan Munir work in the laboratory, collect the samples. Amina Waheed and Muqaddas Majeed work on the manuscript and proofread was done by Sunaina Javed and Muhammad Fakhar while Arslan did proof reading analysis the article, Bilal assist in data analysis, Waseem helped in manuscript writing and data confirmation.



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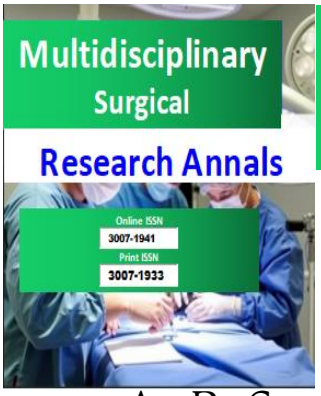

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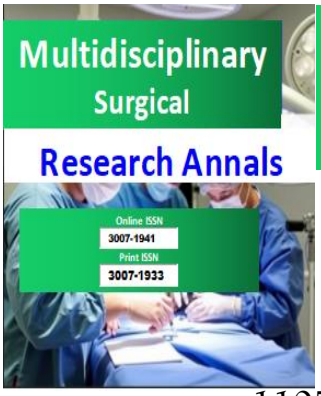

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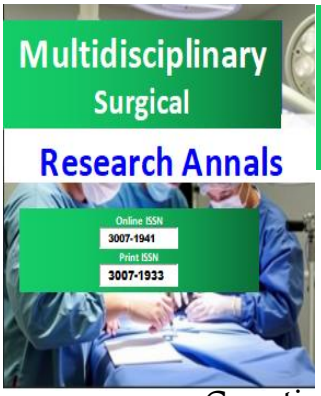

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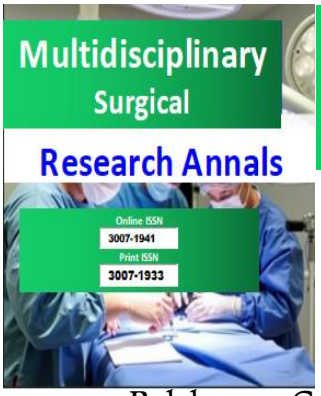

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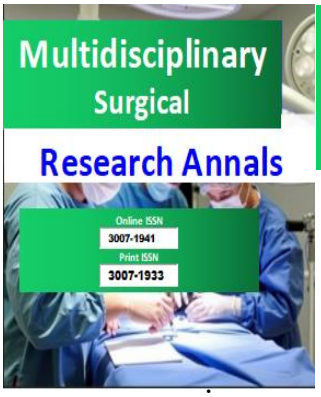

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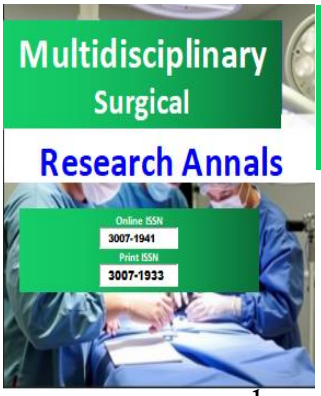

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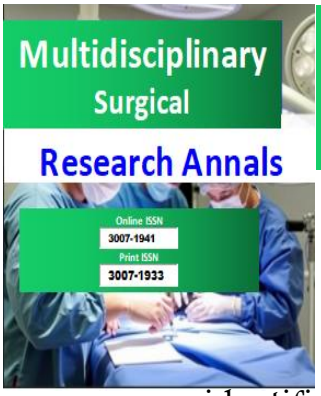

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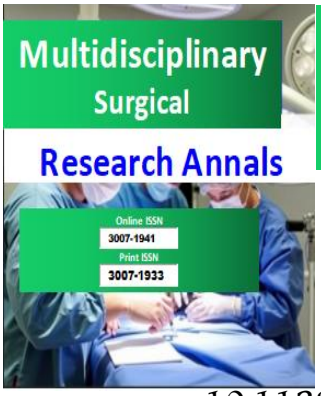

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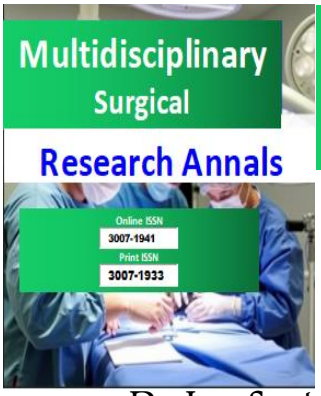

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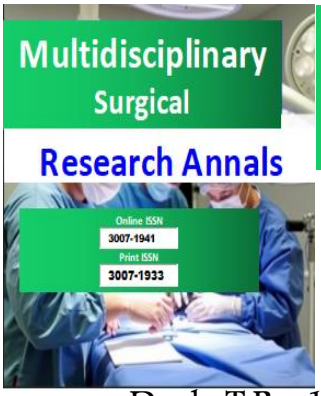

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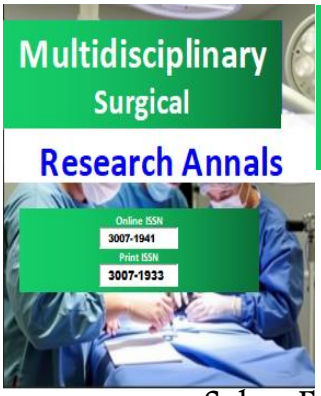

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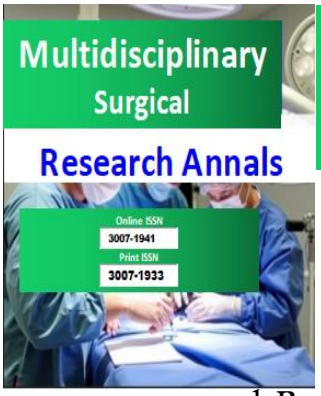

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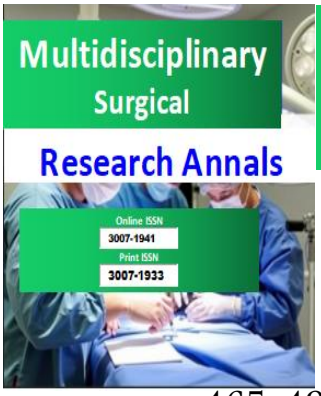

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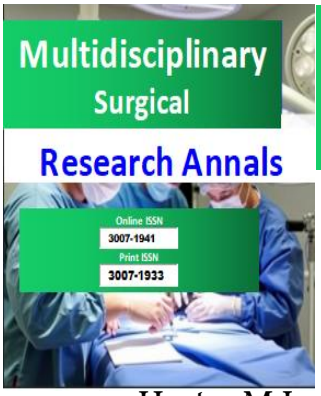

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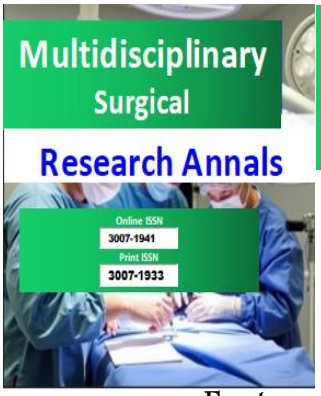

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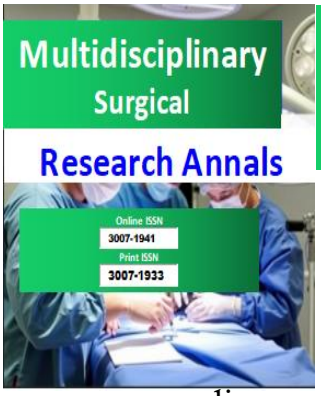

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