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Integrative Analysis of Vibrio Cholerae Genomic Data for Understanding its Pathogenicity and Evolution

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Abstract:- **Cholera remains a significant global health threat, with substantial mortality rates, yet limited information exists on the pathogenicity, genomic data, and evolutionary relationships of *Vibrio cholerae*. This study presents a comprehensive genomic analysis of ten *V. cholerae* strains, examining nucleotide sequence length, virulence factors, pathogenicity islands, and mobile genetic elements. Using tools like NCBI, VFDV, ISLANDviewer, VRprofile, and CLUSTAL OMEGA, the analysis revealed notable variation in nucleotide sequence lengths, with the Amazonia strain and P16 strain showing the highest numbers. Virulence factor analysis identified that some strains, such as Amazonia and C1, possess significantly more virulence factors than others, contributing to cholera pathogenesis. Pathogenicity island analysis showed variability, with some strains like P16 and Amazonia containing more islands, while others, such as strain 0395-B, have fewer, underscoring their role in disease causation. Mobile genetic elements were identified in nine of the ten strains, facilitating the spread of crucial traits across bacterial populations. Evolutionary analysis indicated that all strains share a common ancestor, with Amazonia and strain 1 showing the greatest evolutionary distance from other strains. Additionally, sequence similarity analysis revealed that regions with 80-100% similarity are conserved, while those with less than 80% similarity are non-conserved. These findings offer valuable insights into the genetic diversity, virulence, and evolutionary relationships among *V. cholerae* strains, contributing to a deeper understanding of cholera pathogenesis and potential avenues for intervention.**

Keywords:- *Cholera, Genomic Data, Virulence Factors, Pathogenicity Island, Mobile Genetic Elements, Evolutionary Relationships.*

I. INTRODUCTION

A prevalent class of rod-shaped, Gram-negative bacteria found naturally in freshwater, estuaries, and marine settings is called Vibrio spp. Various physiological and genetic traits are shared by different types of Vibrio's. The two chromosomes, each formed by recombination and horizontal transfer of genes (HTG, or the acquisition of genetic material by transfer from other organisms), split their genomes. Most human infections linked to the natural microbiota of aquatic settings and seafood are caused by Vibrio spp. [1]. Vibrio cholerae, Vibrio parahaemolyticus, Vibrio vulnificus, and Mycobacterium are among the most prevalent infectious agents. Alginolyticus. Infections caused by Vibrio species exhibit a clear seasonal trend, with the majority of cases taking place in warmer seasons. Humans can have a range of signs of viral infections, which are typically brought on by drinking contaminated water or eating raw or undercooked contaminated seafood [2].

The microbial illness Vibriocholerae is contracted by consuming or drinking tainted food or water. The organism that causes the illness is comma-shaped. The acute diarrheal illness known as cholera is caused by the bacteria Vibrio cholerae [3]. Water-borne V. cholerae can spread via vector and reservoir species like bacteria, certain crustaceans, and insects [4]. V. cholerae thrives best in saline water in coastal locations and rivers [5]. High amounts of V. cholerae have also been found in the feces of human cholera carriers. The cholera virus can infect both food and water supplies via these kinds of procedures. After being consumed via the fecal-oral pathway, Diarrhea and dehydration are two indications of illness [6].

The objectives of this study is to, comprehensively analyze genomic sequences of vibrio cholerae strains collected from NCBI, to identify virulence factors, genetic islands, and mobile genetic elements associated with pathogenicity, and to elucidate the evolutionary dynamics, including phylogenetic relationships, population structure, and genetic diversity of V. cholerae.

The outcome of this study is to, Identify the virulence factors, through virulence factors database, insight into evolutionary history, tracking epidemic spread, comparative genomic, and targeted intervention.

II. MATERIALS AND METHODS

➢ *Retrieval of Vibrio Cholerae Strain Genomic Sequences*

- Ten (10) Vibrio cholerae strain sequences were retrieved from the National Center for Biotechnology Information (NCBI) database at https://www.ncbi.nlm.nih.gov. information obtained includes, accession ID, sources, and references in FASTA Format.

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- Virulence factors were retrieved from the Virulence Factor Database (VFDB) at https://www.mgc.ac.cn/VFs/.
- The genetic island was retrieved from the island viewer at https://www.pathogenomics.sfu.ca/islandviewer/.
- Mobile genetic elements of the selected sequences of vibrio cholerae strains were retrieved from VRprofile2 at https://tool2-mml.sjtu.edu.cn/VRprofile/VRprofile.php
- The phylogenic tree was retrieved in order to determine and understand the evolutionary relationships, population structure, and genetic diversity of Vibrio cholerae at https://www.ebi.ac.uk/jdispatcher/msa/clustalo

III. RESULTS

➢ *The Genomic Data of the Ten Strains Obtained from the NCBI was Presented in Table 1.*

Table 1 Genomic Data of Ten Vibrio Cholerae Strains Collected from the NCBI Database

S/N	STRAIN NAME	ACCESSION ID	SOURCE	BASE PAIR
1	Amazonia isolate 3509	EU272902	Vibrio cholerae	49240
2	C1 CTX phage region genomic sequence	KY454839	Vibrio cholerae	26796
3	C2 chromosome 1 phage sequence	KY474414	Vibrio cholerae	23664
4	C7 chromosome 1 phage sequence	KY474410	Vibrio cholerae	28102
5	J6 chromosome 1 phage sequence	KY474413	Vibrio cholerae	17090
6	M25 chromosome 1 phage sequence	KY474419	*Vibrio cholerae*	12885
7	Strain No341 chromosome 1 phage sequence	KY474411	*Vibrio cholerae*	16719
8	P2 chromosome 1 phage sequence	KY474416	*Vibrio cholerae*	14490
9	Strain O395-B class 4 integron, partial sequence	FJ982913	*Vibrio cholerae*	4410
10	P16 chromosome 1 phage sequence	KY474417	*Vibrio cholerae*	21076

Table 1 provides information on genomic areas and genetic sequences of ten strains of the cholera-causing Vibrio cholerae bacteria. These sequences can be easily referred to and studied further because they have been recorded in databases with distinct Accession IDs. The longest sequence, 49,240 base pairs, belongs to Amazonia isolate 3509 and suggests a substantial genomic fragment that may include important genes related to the virulence or survival of the bacterium.

A large number of the sequences come from phage sections found in the Vibrio cholerae genome. Examples of these strains' sequences are C1, C2, C7, J6, M25, P2, and P16. These sequences' base pair counts vary from 12,885 to 28,102, which corresponds to different phage DNA lengths.With 4,410 base pairs, the integron sequence of strain O395-B is the shortest. This truncated region might be a particular resistance gene or one of the other useful genes that the integron has caught.

The virulence factors of ten vibrio cholerae strains were obtained from the VFDB database, and were presented in Table 2

Table 2 Virulence Factors of Vibrio Cholerae

S/N	STRAIN NAMES	VIRULENCE FACTORS	FUNCTION
1	Vibrio cholerae strain Amazonia	Ace (Accessory cholera enterotoxin), ACF(Accessory colonization factor), AI-2(Autoinducer-2), CAI-1(Cholerae autoinducer-1), CT (Cholera toxin), Eps T2SS(Extracellular protein secretion), Flagella	Exhibit sequence homology to coat protein genes. Assisting intestinal colonization. Initiate new cycle of infection. Initiate new cycle of infection. Leading to watery diarrhea. Cause diarrhea by T2SS secretion of cholera toxin. Contribute virulence pathogenicity.
2	Vibrio cholerae strain C1	Ace (Accessory cholera enterotoxin), ACF(Accessory colonization factor), AI-2(Autoinducer-2), CAI-1(Cholerae autoinducer-1), CT (Cholera toxin),	Exhibit sequence homology to coat protein genes. Assisting intestinal colonization. Initiate new cycle of infection. Initiate new cycle of infection. Leading to watery diarrhea and disruption of intestinal cell function.

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		Eps T2SS (Extracellular protein secretion), Flagella, GbpA(N-Acetylglucosamine (GlcNAc)-binding protein A), HAP(Hemagglutinin protease), HlyU, MARTX(Multifunctional autoprocessing RTX toxin), NanH/VCNA(Vibrio cholerae neuraminidase), OmpU, TPC (toxin coregulated pilus), TLH(Thermolabile hemolysin), VCC(Vibrio cholerae cytolysin), VPS(Vibrio polysaccharide), Zot (zonula occuludents toxin)	Cause diarrhea by T2SS secretion of cholera toxin. Contribute virulence pathogenicity of v. cholerae. Binding protein essential for intestinal colonization. Participating in the targeted dehydration of GbPA. Conserve transcriptional virulence gene in v. cholerae. Inducing cytopathic activities in host cell. To encode with pathogenicity island of v. cholerae genome. Mediating attachment for the bacterium to a host cell. To establish colonization in vivo and expressed before CT. Lysis human erythrocytes by a phospholipase B/A2 enzymatic activity. Membrane damaging cell, killing activity. Aids for the improvement of three-dimensional biofilm structure. Exhibit sequence homology to coat protein genes.
3	Vibrio cholerae strain C2	MSHA type IV pili(Mannose-sensitive haemagglutinin type IV pili), RtxA(Repeat in toxin)	Heps in biofilm formation of vibrio cholerae. Inducing host cell rounding and apoptosis.
4	Vibrio cholerae strain C7	MSHA type IV pili(Mannose-sensitive haemagglutinin type IV pili), RtxA(Repeat in toxin)	Heps in biofilm formation of vibrio cholerae. Inducing host cell rounding and apoptosis.
5	Vibrio cholerae strain J6	MSHA type IV pili(Mannose-sensitive haemagglutinin type IV pili), RtxA(Repeat in toxin)	Heps in biofilm formation of vibrio cholerae. Inducing host cell rounding and apoptosis.
6	*Vibrio cholerae* strain M25 chromosome 1 phage sequence	MSHA type IV pili (Mannose-sensitive haemagglutinin type IV pili) RtxA (Repeat in toxin)	Colonization and infection establishment Cytoskeletal damage, and immune evasion
7	*Vibrio cholerae* strain No341 chromosome 1 phage sequence	MSHA type IV pili (Mannose-sensitive haemagglutinin type IV pili) RtxA (Repeat in toxin)	Colonization and infection establishment Cytoskeletal damage, and immune evasion
8	*Vibrio cholerae* strain P2 chromosome 1 phage sequence	MSHA type IV pili (Mannose-sensitive haemagglutinin type IV pili) RtxA (Repeat in toxin)	Colonization and infection establishment Cytoskeletal damage, and immune evasion
9	*Vibrio cholerae* strain P16 chromosome 1 phage sequence	MSHA type IV pili (Mannose-sensitive haemagglutinin type IV pili) RtxA (Repeat in toxin)	Colonization and infection establishment Cytoskeletal damage, and immune evasion
10	*Vibrio cholerae* strain O395-B class 4 integron, partial sequence	Ace (Accessory cholera enterotoxin) ACF (Accessory colonization factor) AI-2 (Autoinducer-2)	Fluid secretion in the intestines Promotes colonization of the host gut

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		CAI-1 (Cholerae autoinducer-1)	Involved in quorum sensing and biofilm formation
		CT (Cholera toxin)	Involved in quorum sensing and biofilm formation
		Eps T2SS (Extracellular protein secretion)	Responsible for the watery diarrhea characteristic of cholera
		Flagella	System for secreting various virulence factors
		GbpA (N-Acetyl glucosamine (GlcNAc)-binding protein A)	Provides motility
		HAP (Haemagglutinin protease)	Facilitates attachment to the intestinal mucosa
		HlyU	Involved in detachment and spread of the bacteria
		MARTX (Multifunctional auto processing RTX toxin)	Involved in the expression of virulence genes
		NanH/VCNA (Vibrio cholerae neuraminidase)	Contributes in host cell damage and immune evasion
		OmpU	Enhances the availability of sialic acid aiding in colonization
		TCP (Toxin-co regulated pilus)	Involved in adherence and immune evasion
		TLH (Thermo labile hemolysis)	Essential for colonization and a receptor for CTXϕ phage
		VCC (Vibrio cholerae cytolysis)	Contributes to hemolysis and tissue damage
		VPS (Vibrio polysaccharide)	Causes cell lysis and intestinal inflammation
		Zot (Zonula occludens toxin)	For biofilm formation and environmental survival
			Increases intestinal permeability and contributing to diarrhea.

Table 2 shows the examination of Vibrio cholerae strains reveals diverse virulence methods, Amazonia and C1 strains include multiple virulence components, including cholera toxin (CT), auxiliary cholera enterotoxin (Ace), and quorum sensing signals like AI-2 and CAI-1. These factors contribute to severe diarrhea, increase colonization, and maintain the bacterial infection cycle. The C2, C7, and J6 strains concentrate on RtxA and MSHA type IV pili. While RtxA causes host cell destruction and apoptosis, which aids in immune evasion and infection establishment, MSHA pili are crucial for biofilm development and adhesion. The virulence profiles of MSHA type IV pili and RtxA, as well as the strains M25, No341, P2, and P16, are similar, which aids in colonization and immune evasion. The O395-B strain is distinguished by a wide range of virulence factors, such as different toxins and proteins linked to biofilms. Through a variety of strategies, this strain effectively evades the immune system, induces severe diarrhea, and encourages gut colonization.

The pathogenicity island of ten strains of vibrio cholerae was obtained from the ISLANDVIEWER database and was presented in Table 3.

Table 3 Pathogenicity Island of Vibrio Cholerae

SN	STRAIN NAME	GENETIC ISLAND /PATHOGENECITY ISLAND
1	*Vibrio cholerae* strain M25 chromosome 1 phage sequence	RstA (replication initiation factor domain-containing protein) RstR (transcriptional repressor) Cep (colonization factor) OrfU (minor coat protein) Ace (accessory cholera enterotoxin) Zot (Zonula occludens toxin) CtxA cholera enterotoxin catalytic subunit CtxA) RstB (Affertcholeram virus CTXphi).
2	*Vibrio cholerae* strain No341 chromosome 1 phage sequence	RstA (replication initiation factor domain-containing protein) RstR (transcriptional repressor) Cep (colonization factor) OrfU (minor coat protein) Ace (accessory cholera enterotoxin) Zot (Zonula occludens toxin) CtxA (cholera enterotoxin catalytic subunit CtxA), Hypothetical protein.
3	*Vibrio cholerae* strain P2 chromosome 1 phage sequence	RstA(replication initiation factor domain-containing protein) RstR (transcriptional repressor) RstB(Affertcholeram virus CTXphi)

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		OrfU(minor coat protein) Zot (Zonula occludens toxin) Cep (colonization factor) CtxA(cholera enterotoxin catalytic subunit CtxA), CtxB(cholera enterotoxin binding subunit CtxB)
4	*Vibrio cholerae* strain P16 chromosome 1 phage sequence	RstA (replication initiation factor domain-containing protein) RstR (transcriptional repressor) Cep (colonization factor) OrfU (minor coat protein) Ace (accessory cholera enterotoxin) Zot (Zonula occludens toxin) CtxA(cholera enterotoxin catalytic subunit CtxA) CtxB (cholera enterotoxin binding subunit CtxB) RstB (Affertcholeram virus CTXphi) Hypothetical protein.
5	*Vibrio cholerae* strain O395-B class 4 integron, partial sequence	CtxA(cholera enterotoxin catalytic subunit CtxA)
6	Vibrio cholerae strain Amazonia	VP120001phagefamilyintegrase VP120002truncatedphagefamily vp12003hypotheticalprotein vp120004 ISTB protein vp120005ISTA VP120008CtransposaseRrfABsubunitA VP1200012CMethyl-acceptingchemotaxis protein
7	Vibrio cholerae strain C1	rstR rstA cep ace orfU zot ctxA ctxB
8	Vibrio cholerae strain C2	rstR rstA cep orfu ctxB
9	Vibrio cholerae strain C7	RStR RStA RStb cep orfu Ace zot ctxA CTXB
10	Vibrio cholerae strain J6	RStR RStA RStb cep orfu Ace zot ctxA CTXB

Table 3 shows that Strains M25, No341, P2, and P16 possess the full complement of genes including RstA, RstR, Cep, OrfU, Ace, Zot, CtxA, and CtxB. While strain O395-B only carries CtxA, suggesting a more restricted genetic profile linked to toxin production, strain P2 also possesses RstB, a gene linked to the Affertcholeram virus CTXphi. While strains C1, C2, C7, and J6 exhibit variations in the presence of the above genes, strain Amazonia includes a variety of genes and proteins, including VP120001 (phage family integrase), VP120002 (truncated phage family),

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VP120003 (hypothetical protein), VP120004 (ISTB protein), VP120005 (ISTA), VP120008 (C transposase RrfAB subunit A), and VP120012 (Methyl-accepting chemotaxis protein). These strains reflect a diverse set of genetic elements.

The mobile genetic element of ten strains of vibrio cholerae was generated from the VRprofile database and was presented in Table 4.

Table 4 Mobile Genetic Element of Vibrio Cholerae

S/N	STRAIN NAMES	MOBILE GENETIC ELEMENTS
1	Vibrio cholerae strain Amazonia	prophage, Iscluster/Tn/ ISVCh3/ch4
2	Vibrio cholerae strain C1	Nil
3	Vibrio cholerae strain C2	Prophage
4	Vibrio cholerae strain C7	Prophage
5	Vibrio cholerae strain J6	Prophage
6	M25 chromosome 1 phage sequence	Prophage
7	strain No341 chromosome 1 phage sequence	Prophage
8	P2 chromosome 1 phage sequence	Prophage
9	strain O395-B class 4 integron, partial sequence	Integron
10	P16 chromosome 1 phage sequence	Nil

Table 4 shows that Amazonia contains various mobile genetic elements, including prophage and several insertion sequences. Strain C1 and P16 lacks mobile genetic elements, while strains C2, C7, M25, No341, P2 and J6 each have prophages. Conversely, strain O395-B features an integrin.

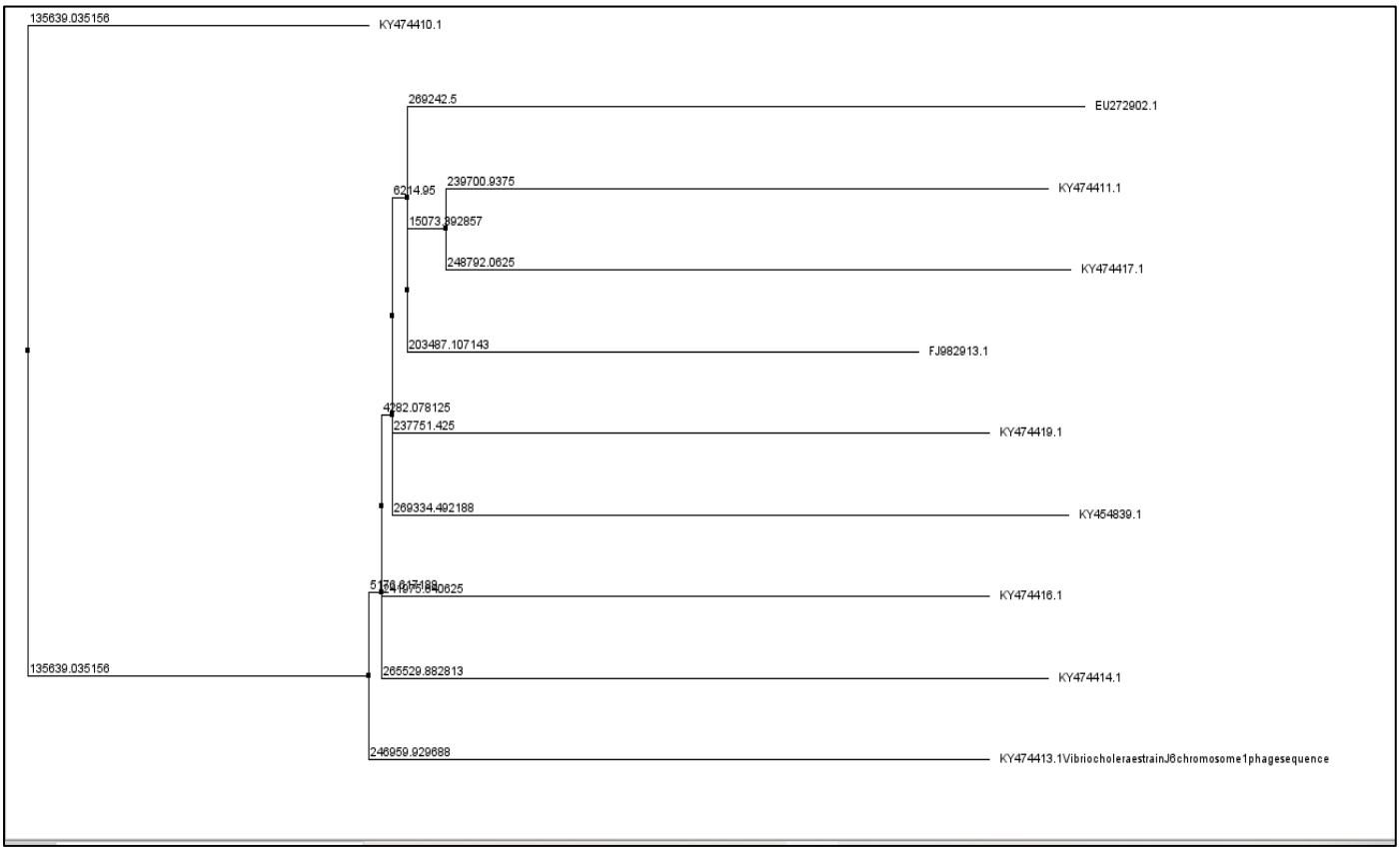

Fig 1 Phylogenic Tree

The phylogenic tree for the whole ten strains of vibrio cholerae was generated from the CLUSTAL OMEGA database, the phylogenic tree were presented in Figure 1

Figure 1: represents the evolutionary relation among the ten strains of vibrio cholerae, they are from the same ancestors, but the distance in a relationship differs from one strain to another.

IV. DISCUSSION

The analysis of the pathogenic potential and genome length of different strains of Vibrio cholerae differ significantly, as shown by the genomic data. Genomic alignment was the main method used to categorize the strains of V. cholerae; this method identified 1763 core genes with a total length of 1,693,138 base pairs out of a predicted 8535 genes, including 105,941 core genomic SNPs. Ten strains

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were classified as non-O1/non-O139, twenty-two as V. cholerae O139, and one hundred and fifty-four as V. cholerae O1 biotype El Tor [7]. Table 1 gives comprehensive information on the genomic data of 10 distinct strains, showing that each strain contributes significantly to pathogenicity, with variations in nucleotide base counts affecting the degree of pathogenicity. As seen in Table 1, strains with more nucleotide bases—like the Amazonia strain—have a larger potential for pathogenicity than strains with fewer bases—like Strain 0395. This Increased in base counts are associated with increased numbers of virulence factors, as each strain's potential virulence factors are correlated with variations in base counts. Additional information suggests that the genomes of V. cholerae strains No341 and P16 contain numerous copies of the CTX Prophage. On chromosome I, however, strains M25 and P2, which have longer sequences, most likely have a single copy of the CTX Prophage [8]. Contrarily, strain O395-B has a partial integron, a vital mobile genetic element that confers antibiotic resistance and prolongs the bacteria's survival in the host [9]. These results are in line with those of Wang H. et al. (2019) and Welch T.J. et al. (2017). And in contradiction with the findings of Kim E.J. [7, 8 ,9].

The pathophysiology of cholera is significantly affected by important pathogenic elements such as cholera toxin (CT) and toxin-coregulated pilus (TCP), that are intimately linked to the onset of severe watery diarrhea [10].Cholera toxin is encoded by the ctxAB gene, which is mostly composed of two RS2 elements with an essential segment. It is a component of the 6.7–6.9 kb lysogenic filamentous bacteriophage CTX. The RS2 region has ORFs for rstR, rstA, and rstB, which are essential for genome replication and the regulatory actions of the CTX phage. In contrast, the core area contains ORFs for cep, orfU, ace, zot, ctxA, and ctxB, which are necessary for phage morphogenesis and bacterial toxicity [11,12]. By changing the intestinal barrier, Zonula occludens toxin (Zot) and accessory cholera enterotoxin (Ace) found in the core region also increase the toxicity of the strains [13]. Numerous strains of Vibrio cholerae, such as ctxA, ctxB, tcpA, ace, hap, and acf, have similar virulence factors, according to analysis of the bacteria [14, 17]. These factors all contribute to the pathogenicity of cholera. The mannose-sensitive hemagglutinin (MSHA) type IV pili and the RtxA protein, for example, are virulence factors of strains M25, No341, P2, and P16. These strains are more pathogenic because they are essential for biofilm formation, host colonization, and cytotoxicity [15, 16]. These strains probably adopt a conserved pathogenic approach to induce cholera by attaching themselves to intestinal cells and releasing toxins that harm host tissues. On the other hand, strain O395-B displays a wider range of virulence factors, such as AI-2 and CAI-1, in addition to additional regulatory components like CT, Zot, Ace, and TCP. According to this diversity, O395-B is a powerful and highly adaptive pathogen that can successfully colonize hosts, evade the immune system, and seriously harm host tissues, all of which can result in severe disease symptoms [13]. It is essential to comprehend the differences in pathogenicity and effects of various Vibrio cholerae strains in order to create focused treatment and prevention plans. The results are consistent with the study carried out by Hsiao et al. [13, 14, 18]. The presence of Pathogenicity islands have been established using DNA sequence recognition using BLAST among Vibrio cholerae species-specific genes, including ompW, the virulence gene ctxA, biotype-specific genes (tcpA, rstR, and ctxB), and O-antigen biosynthesis serogroup-specific genes (wbe O1 and wbf O139) [19]. These "pathogenicity islands" are essential to the development of cholera because they provide the bacteria with the means to infect hosts, evade the immune system, and survive in a variety of settings. For example, the tcp gene cluster, which encodes TCP, a crucial colonization factor, and genes like ctxA and ctxB, which are crucial for the synthesis of cholera toxins, are present on Vibrio pathogenicity island I (VPI-1) and are necessary for cholera pathogenesis [20,21]. Gene clusters known as "pathogenicity islands" are frequently transported laterally and are linked to new traits including antibiotic resistance and pathogenicity [22]. One of the first genetic components that enabled the formation of epidemic V. cholerae strains is the Vibrio pathogenicity island (VPI). It contains genes essential to the development of cholera, such as those responsible for colonization (TCP) and toxin generation (ctxA and ctxB) [23]. Recent research raises the possibility that VPI is phage-encoded and has the ability to replicate as a plasmid, underscoring its significance in V. cholerae's adaptability and pathogenicity [24].

The study's findings showed that the majority of strains—aside from O395-B—had a core set of pathogenicity island genes, which are essential for replication, transcription regulation, colonization, and the synthesis of toxins. These genes include RstA, RstR, cep, OrfU, Ace, Zot, and CtxA. The fact that CtxA is present in every strain highlights how important the protein is to the pathogenicity of cholera since it causes the severe diarrheal symptoms that are typical of the illness. The full cholera toxin (AB5 toxin) in strains P2 and P16, which have both CtxA and CtxB, may cause them to be more lethal and virulent. In the meantime, the discovery of extra putative proteins in strains P16 and No341 raises the possibility of unidentified virulence factors that could heighten the pathogenicity of these strains [13]. Overall, these data show the variety of ways in which Vibrio cholerae strains induce illness; shared virulence genes are crucial for pathogenicity, while distinct genes in some strains suggest possible variations in virulence, adaptability, and host impact. The findings are consistent with the study carried out by Kim and Kaas [19, 25].

Vibrio cholerae's population has changed significantly as a result of changes to the genome, the procurement of integrative mobile components and CTX phage alterations. These are significant mechanisms that influence population changes and the pathogenicity of the bacteria [26, 27]. El Tor strains have mobile genetic elements such VSPI, VSP-II, and RS1, which are critical for CTX phage replication and add to the genetic variety required for the adaptation and development of V. cholerae strains [26]. In order to promote genetic diversity, adaptation, and the transmission of important traits like virulence and antibiotic resistance among bacterial populations, the study found mobile genetic components, such as prophages and integrons, in a diversity

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of V. cholerae strains. For instance, the ctxAB operon and other genes necessary for the production and operation of CTX phage particles are carried by the CTX prophage, which integrates into the bacterial chromosome and is present in strains P2, P16, M25, and No341. The phage repressor protein RstR, which preserves lysogeny and promotes horizontal gene transfer, stabilizes this integration [28, 29]. On the other hand, the integron found in strain O395-B is a form of integrative mobile genetic element (IMGE) that is capable of expressing and capturing gene cassettes, which may include genes that are resistant to antibiotics. Integrons are integrated and duplicated inside the bacterial genome by homologous or site-specific recombination after being transported by conjugation, transformation, or transduction [30, 31]. It has been revealed that strain O395-B carries class 4 and class 2 integrons, which carry antibiotic resistance genes, suggesting that it has the ability to acquire and propagate antibiotic resistance [32].The results of the study show that several strains of V. cholerae differ in the presence of mobile genetic elements. For example, the integrated prophages of M25 and No341 strains have significant lengths and a typical GC content for V. cholerae, indicating the possible existence of numerous genes, such as genes for antibiotic resistance or virulence factors. The prophage of the P2 strain has a little higher GC content, which could suggest distinct evolutionary origins or useful genes that provide extra skills. Conversely, strain P16 does not exhibit any identifiable mobile genetic components, suggesting a reduced capacity for horizontal gene transfer that may impact its virulence and adaptability. These results are consistent with earlier studies conducted by B.M. Davis [28, 33].

A phylogenetic analysis of Studies using different Vibrio cholerae strains found both parallels and discrepancies. [34, 35]. Discovered that the cholera strains under investigation, including those from the seventh pandemic, converged into more closely connected evolutionary relationships; strains J6 and C1 showed a higher degree of evolutionary convergence than strains C7 and M25. Figure 1 of a different study's results, on the other hand, shows a different evolutionary relationship, with strains C7 and J6 showing a closer evolutionary relationship to Amazonia and strains C1 and C2 sharing a closer evolutionary relationship within the same sub-clade as strain C7. The results of this study indicate that strain Amazonia is more distantly related to the other strains. The conclusions of Blake P.A. et al. (2020) and Faruque S.M. et al. (2019) are not supported by these results. On the same lines, Hu D.'s phylogenetic tree [34, 35]. Showed that, in contrast to strains P16, P2, and M25, which have tighter genetic ties, strain 0395-B forms a separate cluster, suggesting a more diverse ancestry from the common ancestor. Out of all the strains, strain 341 was found to be closest to strain 0395-B. The analysis also revealed that KY474411.1 and FJ982913.1 were the two most distinct strains, respectively, and that KY474417.1, KY474416.1, and KY474419.1 constituted a closely linked group, indicating recent common ancestry. Understanding the evolutionary history and pathogenicity of Vibrio cholerae requires an understanding of the genetic diversity highlighted by these phylogenetic trees.

V. CONCLUSION

This work offers thorough understandings of Vibrio cholerae, emphasizing its causes, origins, symptoms, and prevention. It also includes complete genomic information, pathogenicity islands, virulence factors, and mobile genetic elements among various strains. Notably, strain 0395 has the lowest nucleotide sequence count (4,410), while the Amazonia strain has the highest (49,240). The sequence lengths of the remaining strains are average. Virulence factor study shows that strain C1 contains eighteen factors (shared seven with Amazonia) compared to strain Amazonia's seven. Two virulence factors are present in strains C2, C7, and J6, which all contribute to the pathogenesis of cholera. The investigation also shows that these strains contain several pathogenicity islands, underscoring their significance in the spread of cholera. To illustrate their significance in illness causation, strains Amazonia, C1, C2, and J6 each had seven, eight, five, and nine islands, respectively. Significant features among V. cholerae strains are disseminated by mobile genetic components. M25, No341, P2, and P16 are among the eight strains out of ten that have prophages that support their pathogenic processes, which include adhesion, cytotoxicity, and toxin generation. With a wider variety of virulence factors, strain O395-B exhibits the potential for increased pathogenicity, especially in the areas of immune evasion, quorum sensing, colonization, and toxin generation. Integrons have been found in O395-B, which may indicate the development of new virulence characteristics and potential resistance to antibiotics. The research contributes to a better knowledge of cholera pathophysiology and possible therapies by highlighting the genetic diversity, virulence, and evolutionary links among Vibrio cholerae strains. The results highlight how crucial it is to comprehend these genetic components and their evolutionary background in order to create efficient containment strategies for cholera epidemics. These discoveries are essential for creating focused therapies, interventions, and safeguards against disease, as well as for improving our understanding of how various Vibrio cholerae strains adapt and cause illness.

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- *Conflict of Interest*

  Authors declare no conflict of interest

- *Authors Contributions*

  Ramgopal Dhakar led the conceptualization, data analysis, writing and editing the manuscript. Sani Ado Umar and Mubarak Sa'idu were instrumental in collecting and analyzing data, conducting result analysis, and contributing to the manuscript writing. Abdullahi Rabi'u and Ahmad Sadi Shitu significantly contributed to data collection, Mr. Pankaj Kumar Teli, and Aminu Ahmed Wudil. Contributed to reviewing and editing the manuscript. Ensuring the

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robustness of this study titled 'Integrative Analysis of Vibrio cholerae Genomic Data for Understanding its Pathogenicity and Evolution.'"

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