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IMMUNOINFORMATIC APPROACH FOR IDENTIFYING POTENTIAL EPITOPE-VACCINE TARGET AGAINST STRUCTURAL POLYPROTEIN OF CHIKUNGUNYA VIRUS

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ABSTRACT

Background/Aim: Chikungunya virus (CHIKV) continues to be a public health threat in many areas, particularly West Africa, where it is endemic. Herein, it is a big challenge because there are no specific antiviral treatments and limited vaccine accessibility amid recent regulatory challenges and safety concerns for approved vaccine. Given this challenge, this immunoinformatics study aimed to identify potential epitope-based vaccine targets within the structural polyprotein of CHIKV using sequences from Nigerian and Senegalese isolates.

Methodology: Publicly available CHIKV protein sequences were retrieved. The sequences were predicted by use of BepiPred for lineal B-cell epitopes, NetMHCpan-4.1 server, for HLA-A2, -A3, and -B7 supertype-restricted epitopes, and ElliPro tool for conformational B-cell epitopes.

Results: The predicted T-cell and B-cell epitopes are from the most antigenic CHIKV structural polyprotein, with the potential to induce both humoral and cell-mediated immunity. Linear B-cell epitope prediction revealed a broadly antigenic profile across the ~1200-residue polyprotein, with multiple high- (score >1.0) to medium-confidence, (0.5 < score ≤1.0). Retained continuous epitopes (≥5 residues) were predominantly short-to-moderate (5–12 aa), with some extending to 47 aa, and showed high conservation. Strain-specific variations included the unique Nigerian octapeptide KTDGSHDW and the Senegalese nonamer MGQEPNYHE (with minor extension MGQEPNYHEE in Nigeria). In additionally, the repertoire of predicted HLA- A2, A3 and B7 Supertype-restricted T-cell epitopes were identified sharing immunogenic peptide with the predicted lineal B-cell epitopes.

Conclusion: These findings highlight conserved and variant B- and T-cell epitopes in the CHIKV structural polyprotein as promising candidates for multi-epitope vaccine design, offering a cost-effective strategy to enhance humoral immunity against circulating West African variants. The results address diagnostic and therapeutic gaps in CHIKV management and provide a foundation for future experimental validation, including immunogenicity assays and cross-reactivity testing, to support region-tailored prevention in Nigeria, Senegal, and similar endemic regions.

Keywords: *Chikungunya virus*, B-cell, T-cell, immune, conserved epitopes, vaccine, Nigeria.

ABBREVIATIONS

CD-Hit: Cluster Database at High Identity with Tolerance; CHIKV: Chikungunya virus; CHIKF: Chikungunya fever; E1 and E2: Envelope glycoproteins; HLA: Human Leukocyte Antigen; IEDB: Immune epitope database; MHC: Major histocompatibility complex; NK-cells: Natural killer cells;

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NCBI: National Center for Biotechnology Information; NSP: Non-structural viral proteins; PI: Protrusion index

1.1 INTRODUCTION

The *Chikungunya virus* (CHIKV), an arthropod-borne alphavirus classified within the *Togaviridae* family, represents a significant yet neglected public health threat in tropical and subtropical regions, particularly in sub-Saharan Africa [1], [2]. The CHIKV is characterized by a single-stranded, positive-sense RNA genome, and its genomic material spans approximately 11.8 kilobases (kb) [3]. The proteome encoded by its genomes consists of nine distinct proteins; made of four non-structural proteins (nsP1–nsP4) which are essential for viral RNA replication, transcription, capping, and host interaction. While the remaining five are structural proteins (C, E3, E2, 6K, E1) from which the virion capsid and envelope are built [4]. *Chikungunya virus* (CHIKV) was first identified in Tanzania in 1952, and known to cause chikungunya fever (CHIKF), a condition characterized by an acute febrile syndrome, profound arthropathy, myalgia, cephalalgia, and cutaneous eruptions [4], [5].

In the African continent, CHIKV sustains both sylvan (involving non-human primate reservoirs) and urban epidemiological cycles, a factor contributing to its sustained endemic presence in regions with limited infrastructure and resources. Despite its designation as a neglected tropical disease by the World Health Organization (WHO), CHIKV-related research initiatives and public health surveillance efforts remain inadequately supported. This deficiency in resources contributes significantly to under-diagnosis, under-reporting, and considerable diagnostic complexity, particularly in areas where its clinical presentation converges with other prevalent arboviral or parasitic infections such as malaria, dengue, or Zika [1], [5]. Since the first outbreak of CHIKV, there has been recurrent notable infections between 2018 and 2019. Globally, Africa alone accounts for over 2,197 suspected or confirmed cases reported in 2025 [6], [7]. While in Nigeria, recent studies indicate widespread presence of serological evidence for CHIKV exposure, which suggest endemic circulation without large-scale epidemics [8], [9], [10].

The human immune system plays a key role in modulating the progression and subsequent resolution of CHIKV infection, initiating potent intrinsic and adaptive immunological reactions during the acute phase [11]. The early secretion of type I interferons (IFN-α/β), in conjunction with various proinflammatory cytokines (e.g., IFN-γ, IL-6, IL-8) and chemokines (e.g., MCP-1, IP-10), facilitates the recruitment of diverse leukocyte, including macrophages, dendritic cells, natural killer cells (NK-cells), and T lymphocytes, aiming to abate viremia (viral replication and dissemination) [12]. Nevertheless, aberrant immunological activity can precipitate immune-mediated pathology, exemplified by protracted articular inflammation orchestrated by CD4+ T lymphocytes and TNF-α. The neutralizing antibodies directed against the viral envelope glycoproteins (E1 and E2) bestows durable immunity, whereas T-cell recognition sites within both structural and non-structural viral proteins (e.g., NSP2) induce cytolytic effector functions essential for pathogen eradication [5], [13]. Identifying these immunological determinants specifically B-cell and T-cell epitopes is essential for

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elucidating the intricacies of host-pathogen interactions and for the development of epitope-based vaccines. Such vaccines could elicit targeted, cross-protective immunity without inducing autoimmunity or enhancing disease.

Despite the availability of large data in the public repositories, there is no approved vaccine with an established safety profile for CHIKV [5]. Using bioinformatics approaches, researchers can leverage on available tools or develop algorithms where they do not exist to determine antigenic potential, major histocompatibility complex (MHC) binding affinity, and structural modeling to prioritize candidates for experimental validation [14]. Tools such as IEDB, NetMHC, and VaxiJen have been implemented in identifying promiscuous epitopes in CHIKV proteins [15], [16]. This predictive capability significantly contributes to the rational development of multi-component vaccine constructs designed to encompass the diverse Human Leukocyte Antigen (HLA) specificities commonly observed within African demographic cohorts.

In this study, a bioinformatics method was explored to identify and predict both linear and discontinuous B-cell epitopes, alongside MHC class I restricted T-cell epitopes. Here, the Chikungunya virus (CHIKV) structural and non-structural proteins sequences, with a specific focus on viral strains circulating within West Africa. The aim is to highlight epitopes with therapeutic potential, that can be candidates for vaccine development and therapeutic strategy.

2.0 METHOD

2.1 Data Retrieval and Processing

Chikungunya structural polyproteins sequences (as of January 2026) were retrieved from NCBI Virus portal (https://www.ncbi.nlm.nih.gov/labs/virus/vssi/#/), by the use of taxonomy identifier (ID) 37124. Only sequence data for CHIKV viral strains from Nigeria and Senegal representing West Africa countries were available on the virus portal. Additionally, "structural polyprotein," "envelope glycoprotein E1/E2," or "capsid protein." were selected as filters before the download. Duplicate sequences were removed using CD-Hit, a tool for removing redundancy by clustering molecular sequences thereby improving accuracy of analysis [17]. Additionally, partial protein sequences were removed to enhance reproducibility, remove inaccurate and incomplete output of the intended results [18], [19].

2.2 Linear B-cell Epitope Prediction

Linear B-cell epitope prediction was done with BepiPred server (https://tools.iedb.org/main/bcell/) of the immune epitope database (IEDB) [20]. BepiPred can identify both conserved domains of the epitope and continuous stretches of amino acids that bind to antibodies. Epitopes, which had threshold level of ≥ 0.35 and with *kmer* of 9 and above were selected for further analysis. Furthermore, the default sensitivity and specificity values of the prediction was at 0.49 and 0.75, respectively.

2.3 Prediction of T-cell epitopes within the CHIKV structural polyproteins

T-cell epitopes were predicted by use of a local copy of NetMHCpan-4.1 server (https://services.healthtech.dtu.dk/services/NetMHCpan-4.1/) [21], [22], with default parameters. Prediction was done using nonamer peptides length to ensure sensitivity, specificity and to distinguished

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self- from non-self-epitopes [23], [24]; and the representative alleles used of the supertypes [25] are A2 (*A*0201; A*0202; A*0203; A*0204; A*0205; A*0206; A*0207; A*0214; A*0217; A*6802*), A3 (*A*0301; A*1101, A*03101, A*3301, A*3302, A*0301, A*6601, A*7401*), and B7 (*B*0702; B*0703, B*0705, B*1508, B*3501, B*3503, B*4201, B*5101, B*6701, B*7801*). In this study, to accept a supertype predicted, a 50% cut-off was set to determine a putative supertype- specific epitope. The A2, A3, and B7 supertypes were strategically selected as they are well known for their extensive population representation, reportedly encompassing approximately 86% of the general population [26], and are significant to African and other ethnic groups. Putative epitopes that were predicted to have a strong MHC binder (SB) are considered predicted supertype-specific T-cell epitopes.

2.4 Discontinuous/Conformational B-cell epitopes analysis

First, to perform the conformation (discontinuous) B-cell epitopes analysis, the study modelled the 3D structures of the CHIKV proteins used for the linear B-cell epitope prediction using the SWISS-MODEL (https://swissmodel.expasy.org/) [27]. The ElliPro (https://tools.iedb.org/ellipro/) tool was used to evaluate and strengthen the *in-silico* predictions done on CHIKV structural polyproteins as a B-cell epitopes by identifying discontinuous epitopes, which are complex structures formed by non-linear sequences of amino acids, and provide visual map of the antibody-binding epitopes on protein antigens [28]. Here, the model PDB data was input into the ElliPro tool to make predictions by identifying residues that protrude from the globular surface, and then used to calculate a protrusion index (PI) to score potential epitopes.

3.0 RESULTS

3.1 CHIKV protein sequence dataset

A total of 58 *Chikungunya* virus structural polyprotein sequences were retrieved from the NCBI Virus portal. This includes 52 partial envelope polyprotein protein sequences (see Method section), which were removed even after duplicate removal, thus, only 6 protein sequences were relevant for analysis (Table 1). Initially, the removal of duplicate using CD-Hit yielded 11 clusters of non-redundant sequences (Table 1). Here, Nigeria isolate consisting of two sequences each in separate cluster, and the Senegal isolate are grouped into 9 clusters. All the envelope protein were found in one cluster of the Senegal isolates “structural polyprotein (NCBI ID: WWQ34332.1).

Table 1: Number and Distribution of Partial, Non-partial, Redundant, Non- redundant and Geographical Location of CHIKV Sequences

Protein ID	Protein Name	Geographical Isolate	Nature of Seq	Cluster with Evn proteins
ADG95924.1	Structural polyprotein	Nigeria		NA[s]
ADG95885.1	Structural polyprotein	Nigeria		NA[s]
WWQ34332.1	Structural polyprotein, partial	Senegal		AFN27043.1 AFN27044.1 AFN27045.1 AFN27046.1

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				AFN27047.1 AFN27048.1 AFN27049.1 AFN27050.1
WWL43432.1	Structural polyprotein, partial	Senegal	Unidentified aa present	NA^p
WWQ34334.1	Structural polyprotein, partial	Senegal		NA^p
WWQ34346.1	Structural polyprotein, partial	Senegal	Unidentified aa present	NA^p
WWQ34356.1	Structural polyprotein, partial	Senegal		NA^p
ADG95907.1	Structural polyprotein	Senegal		NA^s
ADG95919.1	Structural polyprotein	Senegal		NA^s
ADG95942.1	Structural polyprotein	Senegal		NA^s
ADG95944.1	Structural polyprotein	Senegal		NA^s

NB: NA^s -The only single protein in its cluster
NA^p- Contain multiple proteins in its cluster, and the proteins consist of partial sequence

3.2 Prediction of B-Cell Epitopes

BepiPred analysis of the CHIKV full-length proteins revealed multiple putative linear B-cell epitopes distributed across the Nigerian and Senegalese strain sequences, with both high-confidence regions (score > 1.0) and medium-confidence regions (0.5 < score ≤ 1.0) occurring intermittently along the protein length (Figure 1). Overall, the profile indicates a broadly antigenic protein with several exposed, antibody-accessible segments.

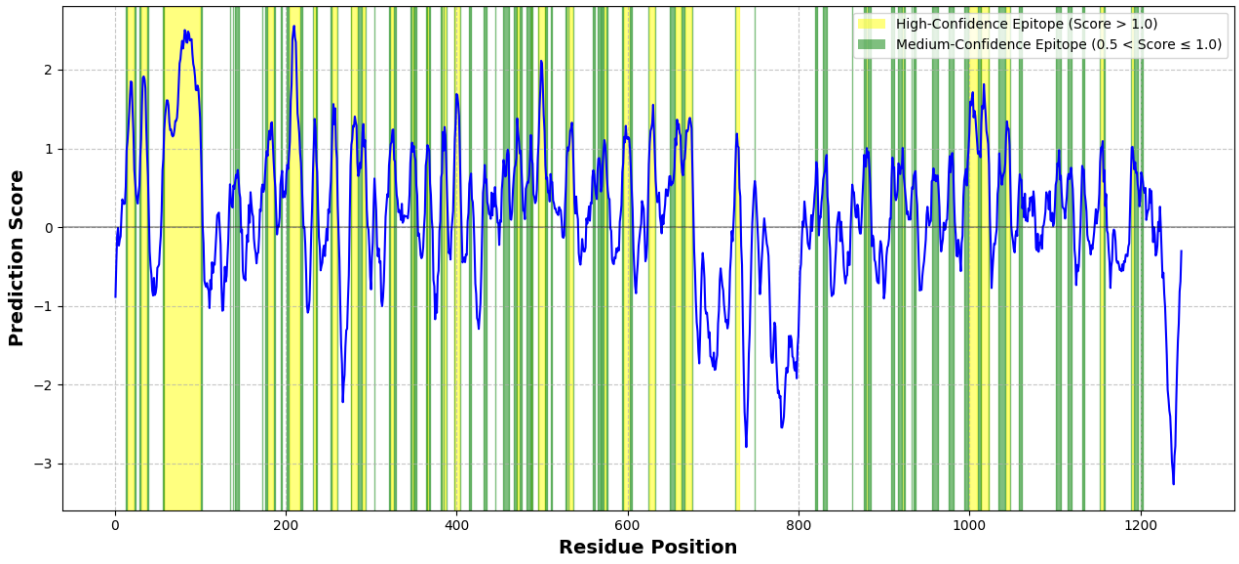

Figure 1. BepiPred prediction of potential linear B-cell epitopes across the protein sequence
BepiPred scores are plotted against residue position (blue line). Predicted epitope regions are

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highlighted as high-confidence (score > 1.0; yellow) and medium-confidence (0.5 < score ≤ 1.0; green). Sequence variation was observed at positions 382–389 (KTDGSHDW; sequence A) and 625–633 (MGQEPNYHE; sequence B).

Since the predicted linear B-cell epitope candidates are distributed across the CHIKV structural polyprotein sequences analyzed, they may exhibit peptide promiscuity, potentially eliciting broad cross-reactive immune responses against multiple CHIKV strains or related alphaviruses. To expand functional consideration, only continuous (consensus) sequences of ≥5 residues (pentapeptides and above) were retained as putative epitope peptides, while isolated residues or discontinuous fragments were systematically excluded (Table 2 and Supplementary Material S1-7). Because the predicted peptide sets were largely overlapping across the dataset, only two representative sequences for West Africa (CHIKV structural polyprotein [Nigeria Strain] (NCBI ID: ADG95924.1) and [Senegal Strain] (NCBI ID ADG95907.1)) were selected for consideration to avoid redundancy (Table 2).

Across both proteins, the majority of predicted epitopes were conserved and occurred as short-to-moderate peptides (5–12 aa), with fewer longer continuous epitope regions extending up to 47 amino acid residues. Despite the overall similarity, two sequence-dependent variations were observed between the representative proteins. CHIKV structural polyprotein [Nigerian Strain] contained the peptide $_{382}$KTDGSHDW$_{389}$, which is absent in all other protein sequences used in the analyses (Table 2 and Supplementary Material S1). Whereas CHIKV structural polyprotein [Senegalese Strain] carried the sequential nonamer residues $_{625}$MGQEPNYHE$_{633}$ but also present in other protein such as the Nigerian strain protein peptide $_{625}$MGQEPNYHEE$_{634}$. These differences indicate that although the predicted B-cell epitope landscape is broadly conserved, specific epitope regions show sequence variability that may influence antibody recognition between the two protein variants. Additionally, these suggest a potential strain-specific antibody recognition and has possible implications for immune targeting and epitope-based vaccine design.

Table 2: Identified linear B-cell epitope (pentapeptides and above) predicted by BepiPred for CHIKV structural polyproteins from Nigerian and Senegalese isolates

ADG95924.1 structural polyprotein [Nigeria]		ADG95907.1 |structural polyprotein [Senegal]	
Peptide	Length	Peptide	Length
PKGET	5	PKGET	5
NTQLS	5	NTQLS	5
ASKKG	5	ASKKG	5
ANEGAR	6	ANEGAR	6
AHTASA	6	AHTASA	6
NEATDGT	7	NEATDGT	7
ELTPGAT	7	ELTPGAT	7
VNRPGYS	7	VNRPGYS	7

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DVEVEGN	7	DVEVEGN	7
PASHTTL	7	PASHTTL	7
KTDGSHDW	8	KTDDSHDW	8
MSSAWTPF	8	MSSAWTPF	8
DAPSVTDM	8	DAPSVTDM	8
ACTHSSDF	8	ACTHSSDF	8
HVKGTIDNA	9	HVKGTIDNA	9
KITPEGAEE	9	KITPEGAEE	9
SHTPADAER	9	SHTPADAER	9
PFHHEPPVI	9	PFHHEPPVI	9
YANGDHAVT	9	MGQEPNYHE	9
PDCGEGHSCH	10	YANGDHAVT	9
CGGSNEGLTT	10	PDCGEGHSCH	10
MGQEPNYHEE	10	CGGSNEGLTT	10
AECKDKSLPD	10	AECKDKSLPD	10
CHPPKDHIVN	10	CHPPKDHIVN	10
YVQSTAATAEE	11	YVQSTAATAEE	11
AHVEKSESCKT	11	AHVEKSESCKT	11
IRPRPRPQRQAG	12	IRPRPRPQRQAG	12
SPHRQRRSTKDN	12	SPHRQRRSTKDN	12
FHSRPQHGKELP	12	FHSRPQHGKELP	12
PKARNPTVTYGK	12	PKARNPTVTYGK	12
RYQPRPWAPRPTIQ	14	RYQPRPWAPRPTIQ	14
VHMPPDTPDRTLMTQ	15	VHMPPDTPDRTLMTQ	15
PAAGTVHVPYSQAPSG	16	PAAGTVHVPYSQAPSG	16
KSDASKFTHEKPEGYYN	17	KSDASKFTHEKPEGYYN	17
FPCSQPPCTPCCYEKEPES	19	FPCSQPPCTPCCYEKEPES	19
KWQYNSPLVPRNAELGDRKGK	21	KWQYNSPLVPRNAELGDRKGK	21
VQYSGGRFTIPTGAGKPGDSGRPIFD	26	VQYSGGRFTIPTGAGKPGDSGRPIFD	26
VYNMDYPPFGAGRPGQFGDIQSRTP ESKDVY	31	VYNMDYPPFGAGRPGQFGDIQSRTP ESKDVY	31
TVPTEGLEVTWGNNEPYKYWPQM STNGTAHGH	32	TVPTEGLEVTWGNNEPYKYWPQM STNGTAHGH	32
VPQQKPRRNRKNKKQRQKKQAP QNDPKQK KQPPQKKPAQKKKKPGRR	47	VPQQKPRRNRKNKKQRQKKQAP QNDPKQK KQPPQKKPAQKKKKPGRR	47

NB: Peptide in bold and underline are equally predicted as potential T-cell epitopes (see Table 3.3)

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3.3 Putative predicted HLA supertype-specific T- cell epitopes

NetMHCpan-4.1 analysis predicted multiple MHC class I supertype-restricted T-cell epitopes across the CHIKV structural polyprotein sequences, with the three commonly occurring supertypes: HLA-A2, HLA-A3, and HLA-B7. The identified predictions were predominantly composed of nonapeptides, consistent with the canonical peptide length preference for MHC class I presentation. Several of the high-ranking nonapeptides (highlighted in the Table 3.3) overlapped with regions previously predicted as linear B-cell epitopes (Table 3.2). For example, the predicted HLA-A3 supertype-restricted epitopes KQKKQPPQK and KQAPQNDPK were found to be contained in the predicted lineal B-cell epitope VPQQKPRRNRKNKKQRQKKQAPQNDP KQKKQPPQKKPAQKKKKPGRR, whereas KSDASKFTH and FTIPTGAGK were located in KSDASKFTHEKPEGYYN and VQYSGGRFTIPTGAGKPGDSGRPIFD predicted B-cell epitope, respectively. However, predicted HLA-B7 supertype-restricted epitopes KPGDSGRPI is located in the predicted B-cell epitope VQYSGGRFTIPTGAGKPGDSGRPIFD. Additionally, RPRPQRQAG, is found in IRPRPRPQRQAG, SPHRQRRST in SPHRQRRSTKDN, and RPWAPRPTI in RYQPRPWAPRPTIQ predicted lineal B-cell epitopes respectively. All these indicates the presence of shared immunogenic hotspots across both humoral and cellular branches of adaptive immunity.

Across the two strains, predicted epitope repertoires were largely conserved for HLA-A2 and HLA-B7, with comparable epitope counts between the Nigerian (NGP1) and Senegalese (SP2) isolates (Table 3.3). In contrast, HLA-A3 supertype epitopes were not consistently represented in the Senegalese isolate, suggesting a strain-dependent reduction or absence of A3-associated peptide binding motifs. Collectively, these results indicate that while CHIKV structural polyproteins maintain broadly conserved T-cell epitope candidates for A2 and B7 supertypes across strains, A3-associated epitope presentation may be more variable between the Nigerian and Senegalese sequences.

Table 3.3: Number of nonapeptide predicted as HLA T-cell restricted epitopes

HLA A2 Supertype specificity/ Allele Count			HLA A3 Supertype specificity/ Allele Count			HLA B7 Supertype specificity/ Allele Count		
T-cell epitope	NGP1	SP2	T-cell epitope	NGP1	SP2	T-cell epitope	NGP1	SP2
RQAGQLAQL	7	7	AQLISAVNK	6	6	RPRPQRQAG	8	8
QLAQLISAV	9	9	TMRAVPQQK	6	6	RPQRQAGQL	9	9
QLISAVNKL	10	10	KQKKQPPQK	6	6	KPAHVKGTI	9	9
SLALPVLCL	5	5	KQAPQNDPK	6	-	KPGDSGRPI	9	9
LLYPDHPTL	10	10	CLVGDKVMK	6	-	SPHRQRRST	7	7
TMTVIIVSV	7	7	KVMKPAHVK	6	6	APCTITGTM	9	9
ATVPFLLSL	9	9	KLAFKRSSK	6	6	CPKGETLTV	9	9
YLWNEQQPL	10	10	CAQIPVHMK	6	-	HPFHHEPPV	9	9
ALIPLAALI	5	5	KSDASKFTH	6	-	VPKARNPTV	9	9
TVIPNTVGV	10	10	FTIPTGAGK	6	6	TPGATVPFL	9	9
SLPDYSCKV	10	10	SGRPIFDNK	6	-	QPLFWLQAL	9	9
ALASAEFRV	10	10	ALSVVTWNK	6	6	IPLAALIVL	9	9
HIPFPLANV	5	5	RMLEDNVMR	6	-	RPGYSPMVL	9	9

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VTLEPTLSL	6	6	LTCSPHRQR	5	-	SPMVLEMEL	9	9
			STKDNFNVY	6	-	TPFDNKIVV	9	9
			NVYKATRPY	6	-	RPAAGTVHV	9	9
			KATRPYLAH	5	-	APSGFKYWL	9	9
			QVSLQIGIK	6	-	RPWAPRPTI	9	9
			GSHDWTKLR	6	-	APRPTIQVI	9	9
			TMGHFILAR	6	-			
			HTCTHPFHH	6	-			
			MTQQSGNVK	6	-			
			TVNGQTVRY	6	-			
			HAAVTNHKK	6	-			
			VTNHKKWQY	6	-			
			KARNPTVTY	6	-			
			STNGTAHGH	6	-			
			LLCCVRTTK	6	-			
			RTTKAATYY	6	-			
			ATYYEAVAY	6	-			
			KTLVNRPGY	6	-			
			TVIPSPYVK	6	6			
			KSLPDYSCK	6	6			
			QLSEAHVEK	6	6			
			KTEFASAYR	6	-			
			ASAKLRVLY	6	-			
			SAWTPFDNK	6	-			
			GQFGDIQSR	6	-			
			IQSRTPESK	6	-			
			YSQAPSGFK	6	-			
			SQAPSGFKY	6	-			
			AIIKYTASK	6	6			
			IIKYTASKK	6	5			
			TTAMSWVQK	6	6			

NB: Those in bold are nonapeptide identified in the predicted lineal B-cell epitopes (see Table 2).

3.4 Analysis of Conformational (Discontinuous) B-Cell Epitopes

Identifying specific site for antigen recognition as in the case of B-cell analysis has a role in vaccine development. More so, B-cell epitopes are broadly classified into two principal forms: linear (also known as sequential) and conformational (also referred to as discontinuous). Empirical evidence indicates that the vast majority of these antigenic determinants are conformational in structure, constituting over 90% of the total [29], [30]. In this study, 3 conformational B-cell epitopes were predicted with the aid of ElliPro tool of IEDB. The epitopes having a protrusion index (PI) score ranges between 0.666 to 0.889. These values are above the optimal coverage of 0.5 PI score combined with a maximum distance (R) of 6Å set as default for ELLiPro. Herein, the highly significant discontinuous epitope was evaluated at 88.9% (PI score: 0.889) and is

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presented in Figure 2(a). The conformational epitopes and their individual amino acid residues, residue position, peptide length, and the PI scores are provided in Table 3.4, conversely their spatial disposition within the three-dimensional structures is visually represented in Figures 2(a)–(c).

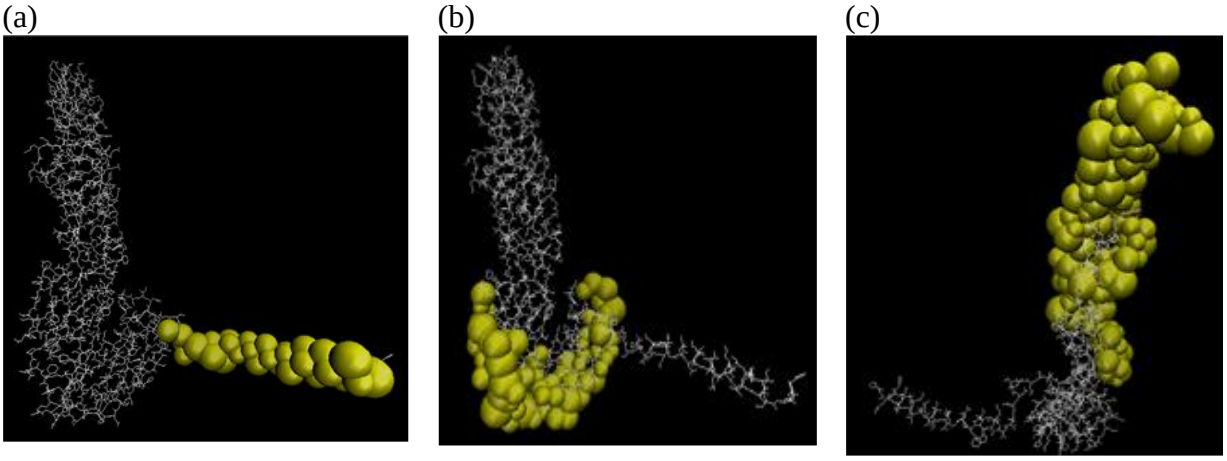

Figure 2: Three-dimensional (3D) representation conformational (or discontinuous) epitopes (a-c) of the antigenic structural polyprotein of CHIKV
Predicted epitopes are shown by yellow surface, and majority of the structural polyprotein is represented in white line

Table 4: Predicted Discontinuous B-cell Epitopes of the structural polyprotein of CHIKV

Epitope No.	Amino acid residues and their positions	No. of residues	PI Score	3D structure
1	D_{1210}, I_{1211}, S_{1212}, T_{1213}, T_{1214}, A_{1215}, M_{1216}, S_{1217}, W_{1218}, V_{1219}, Q_{1220}, K_{1221}, I_{1222}, T_{1223}, G_{1224}, G_{1225}, V_{1226}, G_{1227}, L_{1228}, I_{1229}, V_{1230}, A_{1231}, V_{1232}, A_{1233}, A_{1234}, L_{1235}, I_{1236}, L_{1237}, I_{1238}, V_{1239}, V_{1240}, L_{1241}, C_{1242}, V_{1243}, S_{1244}, F_{1245}, S_{1246}, R_{1247}	38	0.889	Figure 2(a)
2	T_{862}, V_{863}, I_{864}, P_{865}, S_{866}, P_{867}, Y_{868}, V_{869}, K_{870}, C_{871}, C_{872}, G_{873}, T_{874}, A_{875}, E_{876}, C_{877}, K_{878}, D_{879}, K_{880}, S_{881}, L_{882}, P_{883}, D_{884}, Y_{885}, S_{886}, C_{887}, K_{888}, V_{889}, F_{890}, T_{891}, G_{892}, V_{893}, Y_{894}, P_{895}, F_{896}, M_{897}, W_{898}, G_{899}, G_{900}, A_{901}, Y_{902}, C_{903}, F_{904}, C_{905}, D_{906}, A_{907}, E_{908}, N_{909}, T_{910}, Q_{911}, L_{912}, S_{913}, E_{914}, A_{915}, H_{916}, T_{1026}, L_{1028}, V_{1029}, L_{1030}, Q_{1031}, R_{1032}, P_{1033}, A_{1034}, A_{1035}, G_{1036}, T_{1037}, V_{1038}, H_{1039}, V_{1040}, P_{1041}, Y_{1042}, S_{1043}, Q_{1044}, A_{1045}	74	0.778	Figure 2(b)
3	Y_{810}, E_{811}, R_{830}, P_{831}, G_{832}, Y_{833}, S_{834}, P_{835}, M_{836}, Y_{946}, Q_{947}, H_{961}, A_{962}, V_{963}, T_{964}, V_{965}, K_{966}, D_{967}, A_{968}, K_{969}, D_{1090}, I_{1091}, P_{1092}, D_{1093}, A_{1094}, A_{1095}, F_{1096}, T_{1097}, R_{1098}, V_{1099}, V_{1100}, D_{1101}, A_{1102}, P_{1103}, S_{1104},V_{1105}, T_{1106}, D_{1107},	96	0.666	Figure 2(c)

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M_{1108}, S_{1109}, C_{1110}, E_{1111}, V_{1112}, P_{1113}, A_{1114}, C_{1115}, T_{1116}, H_{1117}, S_{1118}, G_{1122}, G_{1123}, V_{1124}, A_{1125}, I_{1126}, I_{1127}, K_{1128}, Y_{1129}, T_{1130}, A_{1131}, S_{1132}, K_{1133}, K_{1134}, G_{1135}, K_{1136}, C_{1137}, A_{1151}, D_{1152}, V_{1153}, E_{1154}, V_{1155}, E_{1156}, G_{1157}, N_{1158}, S_{1159}, Q_{1160}, L_{1161}, Q_{1162}, L_{1169}, A_{1170}, S_{1171}, V_{1178}, C_{1179}, S_{1180}, T_{1181}, A_{1186}, A_{1187}, A_{1188}, C_{1189}, H_{1190}, P_{1191}, P_{1192}, K_{1193}, D_{1194}, H_{1195}, I_{1196}, V_{1197}

4.0 DISCUSSION

Despite recent advancements in *Chikungunya virus* (CHIKV) vaccine development and other prophylactic agents, such as the approval of recombinant VIMKUNYA [31] in multiple regions and the temporary suspension of IXCHIQ [32] due to safety concerns in elderly populations, the clinical management of CHIKV infection continues to encounter substantial limitations [33]. These include a notable absence of specific antiviral therapeutic agents, constrained availability of prophylactic measures in resource-limited environments, and persistent deficiencies in epidemiological surveillance mechanisms, which exacerbate the under-ascertainment of cases during outbreak periods. Such difficulties are particularly pronounced across the sub-Saharan African continent, where recurring transmission cycles in 2024 - 2025 have underscored the prevailing reliance on symptomatic relief and vector abatement strategies. This situation consequently emphasizes the critical imperative for novel, context-specific interventions, such as advanced vaccine platforms like epitope-based candidates [33], [34]. It is important to note that despite using the structural polyprotein of the CHIKV, the polyprotein is basically consist of Capsid (C), E3, E2, 6K, and E1 proteins, which are responsible for the viral machinery and propagation [35], [36].

The immunoinformatic analysis in this study identified a curated dataset of six relevant CHIKV structural polyprotein sequences from Nigerian and Senegalese isolates after filtering out partial and redundant entries, revealing 11 non-redundant clusters via CD-Hit. This limited yield emphasizes the scarcity of complete genomic data for West African strains, which may contribute to gaps in understanding regional viral diversity and hinder tailored therapeutic strategies. BepiPred predictions demonstrated a broadly antigenic profile across the polyproteins, with multiple high-confidence (score >1.0) and medium-confidence (0.5 < score ≤1.0) linear B-cell epitopes distributed intermittently, indicating several antibody-accessible regions suitable for immune targeting. Retaining only continuous epitopes of ≥5 residues minimized fragmentation, yielding short-to-moderate peptides (5–12 aa) alongside longer stretches up to 47 aa, which aligns with typical immunogenic motifs in *Alphaviral* envelope proteins [37].

Notably, the analysis uncovered strain-specific variations, such as the unique octapeptide $_{382}$KTDGSHDW$_{389}$ in the Nigerian isolate which was not observed in Senegalese sequences. Conversely, a nonamer ($_{625}$MGQEPNYHE$_{633}$) present in the Senegalese strain displayed a minor extension ($_{625}$MGQEPNYHEE$_{634}$) in the Nigerian variant. These observed dissimilarities suggest the potential for differential antibody recognition, which may

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elucidate variations in immune responses or patterns of disease outbreaks in West Africa. Such insights are crucial for informing the development of multi-epitope vaccines that incorporate both invariant and variable regions to achieve broad-spectrum protection. Furthermore, the substantial conservation of the epitope repertoire supports the viability of epitope-centric approaches to overcome current therapeutic and preventative limitations, such as vaccine-associated reactogenicity and inadequate immunization coverage among vulnerable populations [38].

Building on the identification of conserved and strain-specific linear B-cell epitopes in West African CHIKV structural polyproteins, such as the unique Nigerian octapeptide $_{382}$KTDGSHDW$_{389}$ and the Senegalese nonamer $_{625}$MGQEPNYHE$_{633}$ (with its extended variant in Nigeria), integrating T-cell epitope predictions could enhance vaccine efficacy by eliciting robust cellular immunity alongside humoral responses. *In silico* analyses using tools like NetMHCpan and NetMHCIIpan on the same representative sequences (e.g., NCBI IDs: ADG95924.1 [Nigeria] and ADG95907.1 [Senegal]) reveal potential MHC class I epitopes overlapping with B-cell regions, particularly in the E2 glycoprotein, where short 8–11 aa peptides exhibit high binding affinities to prevalent African HLA alleles (e.g., HLA-A*02:01), promoting cytotoxic clearance of infected cells. Similarly, when considering MHC class II epitopes, often 13–18 aa in length, align with medium-confidence B-cell sites (scores 0.5–1.0), facilitating T-helper activation that boosts antibody production and long-term memory against chronic arthralgia common in regional outbreaks [39]. The interplay between B- and T-cell epitopes is mutually reinforcing: B-cell predictions highlight surface-exposed antigenic hotspots that may encompass T-cell motifs, enabling multi-epitope constructs for balanced immunity, while T-cell epitopes could amplify responses to variant B-cell regions like KTDGSHDW, addressing strain-specific challenges in Nigeria and Senegal. This bidirectional relevance underscores the potential for comprehensive epitope-based vaccines to mitigate CHIKV management shortfalls in endemic areas, though experimental validation (e.g., ELISPOT assays) is essential to confirm immunogenicity.

The conformational (discontinuous) B-cell epitope prediction complements the linear B-cell analysis by identifying antibody-binding sites dependent on the 3D structure of the CHIKV structural polyprotein, which often constitute the majority of neutralizing epitopes in envelope proteins like E2 and E1. Several discontinuous ($_{1210}$DISTTAMSWVQKITGGVGLIVAVA ALILIVVLCVSFSR$_{1247}$; $_{862}$TTVIPSPYVKCCGTAECKDKSLPDYS CKVFTGVYPFMWGGAYCFCDAENTQL SEAH$_{916}$; $_{1026}$TQLVLQRPAAGTVHVPYSQA$_{1045}$; $_{810}$YERPGYSPM$_{836}$; $_{946}$YQ$_{947}$; $_{961}$HAVTVKDAK$_{969}$; and $_{1090}$DIPDAAFTRVVDAPSVTDMSCEVPA CTHSGGVAIIKYTASKKGKCADVEVEG NSQLQLASVCSTAAACHPPKDHIV$_{1197}$) clusters spatially overlapped or encompassed the linear hotspots, suggesting these variable motifs contribute to native antigenic surfaces. Overall, the conformational profile exhibited high conservation of immunodominant sites, reinforcing the polyprotein's vaccine target suitability despite minor sequence variations in West African isolates. Therefore, this integrated methodology, leveraging both

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linear and conformational epitope analyses, provides a comprehensive elucidation of the antigenic profile. Specifically, linear epitope predictions delineate sequential motifs relevant for adaptable or diagnostic contexts, whereas analyses of discontinuous epitopes reveal biologically pertinent, folded structures pivotal for immune neutralization. The strategic incorporation of these diverse epitope classes into multivalent vaccine designs is posited to enhance protective humoral immunity within populations in Nigeria and Senegal. Nevertheless, empirical validation through advanced techniques, such as cryo-electron microscopy or monoclonal antibody binding assays, remains imperative to ascertain both surface accessibility and functional efficacy.

While this *in silico* framework provides a cost-effective pipeline for epitope prioritization, limitations include reliance on predictive algorithms without experimental validation (e.g., ELISA or neutralization assays) and the exclusion of conformational epitopes, which may overlook key immunodominant sites. Future studies should validate these candidates *in vitro* and *in vivo*, potentially integrating T-cell epitopes for comprehensive vaccine constructs, to advance CHIKV control in endemic regions.

4.1 CONCLUSION

This immunoinformatics study identified potential epitope-based vaccine targets in the structural polyprotein of *Chikungunya virus* (CHIKV) from West African isolates. B-cell epitope prediction showed a broadly antigenic profile with intermittent high-confidence and medium-confidence regions across the sequence, indicating multiple exposed, antibody-accessible segments. More so, strain-specific variations exist in the Nigerian sequences compared to other sequences in West Africa (such as Senegalese isolate), suggesting differential antibody recognition and implications for region-tailored immune targeting. Also, linear B-cell epitopes shows some overlap or lie near T-cell hotspots, enabling multi-epitope vaccines that may stimulate both humoral and cellular arms. These conserved and variant B-cell and T-cells epitopes in the structural polyprotein provide promising candidates for multi-epitope vaccine design to enhance protection against circulating CHIKV variants in Nigeria and Senegal, addressing gaps in current management strategies. Experimental validation is recommended to confirm immunogenicity and cross-reactivity.

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Authors' Contributions

SAJ: Developed and designed the research idea, conducted the research and wrote the manuscript

Consent: All author whose name appeared on this manuscript gave there consent for publication of the fidings in this paper.

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