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Database-sourced Virulence Factor Comparison between strains of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*

Chlamydia trachomatis ve *Neisseria gonorrhoeae* Suşları Arasındaki Virülans Faktörü Karşılaştırması

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Abstract / Ozet

According to the predictions of the World Health Organization, Chlamydia trachomatis and Neisseria gonorrhoeae were two of the most prominent pathogenic bacteria responsible for increasing emergence of sexually transmitted infections. These two bacteria were repeatedly reported as the most serious challenges in public health problems. Both bacteria have similar infection sites and clinical synopses, and reported for co-infections, despite the fact of being from distinct phyla and having distinct life-cycles. Extensive research revealed diverse array of virulence factors for these bacteria, and each of them having different classes of virulence factors appropriate for its life-cycle and survival. In this research curated strains of C. trachomatis and N. gonorrhoeae present in the Virulence Factor Database of the National Institute of Pathogen Biology in China were used for proteome-based intra-genera comparison, which revealed virulence factor class distinctness between the two species. Comparisons were revealed strain uniformity in C. trachomatis but strain variation in N. gonorrhoeae along with pronounced genetic complexity in N. gonorrhoeae virulance factors. However, obtained results revealed absences of related genes for virulance factors in C. trachomatis despite the presence of coding sequences in strains, and absences of coding sequences in N. gonorrhoeae FA 1090 strain. Results also revealed limited amount of virulence factor classes for C. trachomatis contrary to extensive literature reports and multigenic factors in certain virulence factors in N. gonorrhoeae strains due to the presence of multiple coding sequences. Overall, this research was revealed potential targets for further genomics research and emphasized the need of embracing multi-omics approaches in clinical microbiology studies.

Dünya Sağlık Örgütü'nün tahminlerine göre, Chlamydia trachomatis ve Neisseria gonorrhoeae, cinsel yolla bulaşan enfeksiyonların artan yaygınlığından sorumlu en önemli patojenik bakterilerden ikisidir. Bu iki bakteri, halk sağlığı sorunlarında en ciddi zorluklar olarak defalarca rapor edilmiştir. Her iki bakteri de benzer enfeksiyon bölgelerine ve klinik özetlere sahiptir ve farklı filumlardan olmalarına ve farklı yaşam döngülerine sahip olmalarına rağmen, birlikte enfeksiyonlar için rapor edilmiştir. Kapsamlı araştırmalar, bu bakteriler için çeşitli virülans faktörlerini ortaya koymuş ve her birinin yaşam döngüsüne ve hayatta kalmasına uygun farklı virülans faktörü sınıflarına sahip olduğunu göstermiştir. Bu araştırmada, Çin'deki Ulusal Patojen Biyolojisi Enstitüsü'nün Virülans Faktörü Veritabanı'nda bulunan C. trachomatis ve N. gonorrhoeae'nin seçilmiş suşları, proteom tabanlı cins içi karşılaştırma için kullanıldı ve bu da iki tür arasında virülans faktörü sınıfı farklılığını ortaya çıkardı. Karşılaştırmalar, C. trachomatis'te suş homojenliğini, N. gonorrhoeae'de ise suş varyasyonunu ve N. gonorrhoeae virülans faktörlerinde belirgin genetik karmaşıklığı ortaya koydu. Ancak elde edilen sonuçlar, suşlarda kodlama dizilerinin varlığına rağmen C. trachomatis'te virülans faktörleriyle ilgili genlerin bulunmadığını ve N. gonorrhoeae FA 1090 suşunda kodlama dizilerinin bulunmadığını ortaya koymuştur. Sonuçlar ayrıca, kapsamlı literatür raporlarının aksine C. trachomatis için sınırlı sayıda virülans faktörü sınıfı ve N. gonorrhoeae suşlarında birden fazla kodlama dizisinin varlığı nedeniyle bazı virülans faktörlerinde çok genli faktörler olduğunu göstermiştir. Genel olarak, bu araştırma, daha ileri genomik araştırmalar için potansiyel hedefleri ortaya koymuş ve klinik mikrobiyoloji çalışmalarında çoklu omik yaklaşımların benimsenmesinin gerekliliğini vurgulamıştır.

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Introduction

In the context of bacterial sexually transmitted infections (STI), two bacteria species are standing in front, which are Chlamydia trachomatis and Neisseria gonorrhoeae [1]. They are both reported to be major public health concerns as the World Health Organization (WHO) in 2020 had estimated global infection rates reaching to 128.5 million for C. trachomatis, and 82.4 million for N. gonorrhoeae [2]. Epidemiological studies also revealed concerning increases in infection rates over the years, particularly in the US [3]. C. trachomatis, which is an obligate intracellular bacterium, is known to cause the most prominent of STIs that is chlamydia, and can infect different sites including genital tract, rectum, pharynx, and conjuctiva, favoring females over males. N. gonorrhoeae, which is a gram (-) diplococcus, is known as the causative agent for second most prominent STI, the gonorrhea, and, similar to C. trachomatis, can infect different sites including urogenital tract, rectum, pharynx, and conjunctiva [1,2,4]. Both bacteria are also the leading causes for ophthalmia neonatorum, where C. trachomatis is known to be more prominent [5]. Again, aside from more apparent acute symptoms, both bacteria are associated with pelvic inflammatory disease (PID), and it's progressed form that is known as Fitz Hugh-Curtis syndrome [6]. By their causative roles in PID, and their infection mechanisms, both bacteria were also implied for their potential roles in development of carcinogenesis, particularly in ovarian cancer developments [7]. It was reported that most of the clinical cases provided co-infections with both bacteria, and thus the necessity of multiplex PCR-based approaches was emphasized for precise diagnosis [3]. It was also reported, that C. trachomatis not always revealed clinical symptoms, and may cause asymptomatic infections leading to persistence and diagnostic gaps [4]. Overall, with their exceedingly high rates in prevalence, tendency in co-infection, and ongoing persistence, these two bacteria are still one of the most pressing concerns in general public health.

With its unique biphasic development cycle that involves alternations between infectious elementary body and replicative reticulate body, C. trachomatis contains numerous virulence factors, and these virulence factors have reported to have a complex interaction [8,9]. C. trachomatis was reported to deviate from typical norms for bacterial fitness by uniquely coordinating gene expressions and pathogenic pathways to employ its diverse set of virulence factors to manipulate host cell biology [10]. Molecular microbiology studies revealed that C. trachomatis employs different virulance factors, particularly having a highly complex mechanism of effector deliverance by type III secretion system (T3SS), which is also the known primary virulance mechanism. Aside from T3SS, C. trachomatis also reported to have mechnisms for antigenic variation, plasmid-encoded virulence factors, and intracellular metabolic adaptations [8,9]. N. gonorrhoeae also has diverse set of virulence factors, mostly typical for gram (-) bacteria, yet with multifactorial aspects and high genetic diversity for its virulence factors, which lead to making N. gonorrhoeae rather unique pathogen that deviates from pathogenic stereotypes. Clinical and molecular microbiology studies were extensively conducted on both bacteria due to their prominent roles in public health [2,11]. Particular focus was given on virulence factors, which enables bacteria to develop infection in host organisms, hence are keys for the manifestation of clinical symptoms [8,9]. Studies over time reported that C. trachomatis contains highly specialized and intricate virulence factors, possibly due to being an obligate intacellular bacterium, which broadly encompasses Type III Secretion System and its secreted effectors [10], Chlamydial plasmid and plasmid-encoded virulence factors that include Pgp proteins [8,9], Polymorphic Membrane Proteins, Phospholypase D family genes that lead to HKD-LPD proteins, and membrane vesicles [12]. However, Chlamydia trachomatis also reported to have complex mechanisms involving immune modulation, metabolic virulence, stress adaptation, and persistent growth forms to facilitate it's peculiar, hard-to-diagnose infection successes [10,14]. When it comes to N. gonorrhoeae, reported virulence factors are limited compared to Chlamydia trachomatis, yet with pronounced complexity, which bradly include Type IV Pili function [3], Opacity-associated (Opa) proteins [6], Porin Protein (PorB) [6], IgA1 Protease [15], and Lipooligosaccharide (LOS) [7]. However, N. gonorrhoeae was reported to have more specialized mechanisms for infection development that include molecular mimicry [7], complement evasion [1], and antigenic variation [1], (Dubbink et al., 2018). Additionally, alternative virulance mechanisms are still an ongoing research trend for N. gonorrhoeae, which particularly focusing on Iron-transport systems [11].

Despite being from different phyla and evolutionarily distant, these two bacteria are responsible similar infections and similar clinical symptoms, also targeting same anatomical sites, yet by utilizing different and quite specialized virulence factors. This peculiar situation necessitates a proteomics-based virulence factor comparison between C. trachomatis and N. gonorrhoeae species to evaluate virulence factor composition between species, which would enable directed research approaches and specific target-based clinical studies in these species. Therefore, in this research, the primary aim was to compare known virulence factors of these two bacteria intra-genus proteomics-level to reveal prospecting specific targets for further directed research, which include novel or advanced diagnostics and targeted treatment strategies.

2. Materials & Methods

2.1. The Platform and Tool for Comparison

For the purposes of this research, the Virulence Factor Database (VFDB) and its integrated analysis tools were chosen. VFDB is an online database for virulence factors specifically for pathogenic bacteria that provides an integrated platform for the comprehensive coverage, characterization, and

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interactions of bacterial virulence factors, which was established in 2004 by the National Institute of Pathogen Biology in China [16]. VFDB provides integrated analysis tools for the investigations of bacterial virulence factors in and between species, along with anti-virulence investigation tools and virulence factor prediction analysis workflows. Currently, VFDB contains 12189 virulence factors across 74 genera of pathogenic bacteria with 966 strains involved [17]. Here, in this research, Intra-genera Comparison tool of VFDB were selected for C. trachomatis and N. gonorrhoeae species.

2.2. Strain Selection for Comparison

VFDB contains its own curated selection of strains for pathogenic bacteria genera, which encompasses all the known pathogenic bacteria to date. While VFDB also enables users to supply out-sourced genomes or sequences for downstream analysis [16,17], for the purposes of this research, readily available curated strains of C. trachomatis and N. gonorrhoeae were used. The strains of C. trachomatis included in VFDB were C. trachomatis 434/Bu (serovar L2), C. trachomatis A/HAR-13(serovar A), C. trachomatis D/UW-3/CX (serovar D), and C. trachomatis L2b/UCH-1/proctitis (serovar L2b). The strains of N. gonorrhoeae included in VFDB were N. gonorrhoeae FA 1090 and N. gonorrhoeae NCCP11945.

3. Results

3.1. Reported Virulence factors and associated genes for Chlamydia trachomatis strains

Intra-genera Virulence Factor Comparison tool that was run on C. trachomatis strains revealed two classes of virulence factors, which were protease that has single factor, and secretion system that has 16 factors for Type III Secretion System Effectors, and 29 factors for Type III Secretion System along with related genes for virulence factors and genes of the detected factors on strain chromosomes. The results revealed that all strains of C. trachomatis have associated genes for the detected virulance factors on their chromosomes. However, the results also revealed that single virulence factor under Protease class, CPAF, one virulence factor in Type III Secretion System, and six virulence factors in Type III Secretion System Effectors have no related genes to associate. The results were given in Table 1 as obtained from the database.

3.2. Reported Virulence factors and associated genes for Neisseria gonorrhoeae strains

Intra-genera Virulence Factor Comparison tool that was run on N. gonorrhoeae strains revealed eight classes of virulence factors, which were classes of adherence, efflux pump, immune modulator, invasion, iron uptake, protease, stress adaptation, and toxin. Of these classes, largest amount of virulence factors was in adherence class with Type IV Pili and LOS synthesis factors having largest amount of related genes, yet classes of iron uptake, stress adaptation, and invasion also observed to be dominant. Multigenic relationship in virulence factors were observed highest in Type IV pili (22 related genes), which were followed by LOS synthesis (11 related genes), ABC transport, TON system, Manganese Transport System, and MtrCDE with 3 related genes each. Results revealed that while N. gonorrhoeae NCCP11945 strain contains all the detected virulence factors, N.gonorrhoeae FA 1090 strain observed to not having 7 virulence factors that include IgtA-related LOS syntesis factor, Phosphoethanolamine modification factor, pilE-related and pilS-related Type IV Pili, Class 5 outer membrane protein factor, and Lactoferrin-binding protein factor. Another interesting result was the observation of more than one genes for a given virulence factor in N. gonorrhoeae NCCP11945 strain as seen in pilC-related Type IV pili, pilE-related Type IV pili, and pilS-related Type IV pili. Similarly, Opacity Protein virulence factor were observed with multiple genes in both strains. The results were given in Table 2 as obtained from the database.

3.3. Comparison of Virulence Factors and associated genes

The results have revealed that, as seen from both Table 1 and Table 2, C. trachomatis and N. gonorrhoeae share only one virulence factor class that is the class of Protease, yet with different virulence factors, which are CPAF for C. trachomatis, and IgA Protease for N. gonorrhoeae. Aside from the class of Protease, virulence factor classes reported in two bacteria were observed as separate and shown no sharing. Because of this, also related and associated genes were different.

Table 1. Virulence Factors reported for Chlamydia trachomatis strains

Chlamydia						
VFclass	Virulence factors	Related genes	C.trachomatis 434/Bu(serovar L2) chromosome (NC_010287)	C.trachomatis A/HAR-13(serovar A) chromosome (NC_007429)	C.trachomatis D/UW-3/CX(serovar D) chromosome (NC_000117)	C.trachomatis L2b/UCH-1/proctitis(serovar L2b) chromosome (NC_010280)
Protease	CPAF	-	CTL0233	CTA_0936	CT858	CTLon_0233
Secretion system	Type III secretion system effectors	--	CTL0219	CTA_0923	CT847	CTLon_0219
		-	CTL0063	CTA_0755	CT694	CTLon_0063
		-	CTL0480	CTA_0250	CT228	CTLon_0476
		-	CTL0481	CTA_0251	CT229	CTLon_0477
		-	CTL0223	CTA_0927	CT850	CTLon_0223
		-	CTL0338	CTA_0087	CT082	CTLon_0333
		NUE	CTL0106	CTA_0799	CT737	CTLon_0106
		inaC	CTL0184	CTA_0885	CT813	CTLon_0184
		incA	CTL0374	CTA_0126	CT119	CTLon_0370
		incB	CTL0484	CTA_0254	CT232	CTLon_0480
		incC	CTL0485	CTA_0255	CT233	CTLon_0481
		incD	CTL0370	CTA_0122	CT115	CTLon_0366
		incE	CTL0371	CTA_0123	CT116	CTLon_0367
		incG	CTL0373	CTA_0125	CT118	CTLon_0369
		tarp	CTL0716	CTA_0498	CT456	CTLon_0712
		tepP	CTL0255	CTA_0001	CT875	CTLon_0250
	Type III secretion system	-	CTL0847	CTA_0634	CT584	CTLon_0841
		cdsC	CTL0043	CTA_0731	CT674	CTLon_0043
		cdsD	CTL0033	CTA_0721	CT664	CTLon_0033
		cdsE	CTL0034	CTA_0722	CT665	CTLon_0034
		cdsF	CTL0035	CTA_0723	CT666	CTLon_0035
		cdsG	CTL0036	CTA_0724	CT667	CTLon_0036
		cdsJ	CTL0822	CTA_0609	CT559	CTLon_0816
		cdsL	CTL0824	CTA_0611	CT561	CTLon_0818
		cdsN	CTL0038	CTA_0726	CT669	CTLon_0038
		cdsO	CTL0039	CTA_0727	CT670	CTLon_0039
		cdsP	CTL0040	CTA_0728	CT671	CTLon_0040
		cdsQ	CTL0041	CTA_0729	CT672	CTLon_0041
		cdsR	CTL0825	CTA_0612	CT562	CTLon_0819
		cdsS	CTL0826	CTA_0613	CT563	CTLon_0820
		cdsT	CTL0827	CTA_0614	CT564	CTLon_0821
		cdsU	CTL0346	CTA_0096	CT091	CTLon_0342
		cdsV	CTL0345	CTA_0095	CT090	CTLon_0341
		cdsZ	CTL0655	CTA_0433	CT398	CTLon_0651
		copB2	CTL0236	CTA_0939	CT861	CTLon_0236
		copB	CTL0841	CTA_0628	CT578	CTLon_0835
		copD	CTL0842	CTA_0629	CT579	CTLon_0836
		copN	CTL0344	CTA_0094	CT089	CTLon_0340
		mcsc	CTL0512	CTA_0282	CT260	CTLon_0508
		pkn5	CTL0042	CTA_0730	CT673	CTLon_0042
		scc1	CTL0343	CTA_0093	CT088	CTLon_0339
		scc2	CTL0839	CTA_0626	CT576	CTLon_0833
		scc3	CTL0237	CTA_0940	CT862	CTLon_0237
		scc4	CTL0032	CTA_0720	CT663	CTLon_0032
		slc1	CTL0299	CTA_0047	CT043	CTLon_0294

Table saved from VFDB (http://www.mgc.ac.cn/VFs/) [Fri Apr 24 04:34:31 2026]

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Table 2. Virulence Factors reported for Neisseria gonorrhoeae

Neisseria				
VFclass	**Virulence factors**	**Related genes**	**N.gonorrhoeae FA 1090**	**N.gonorrhoeae NCCP11945**
			chromosome (NC_002946)	**chromosome (NC_011035)**
Adherence	Adhesion and penetration protein	app	NGO2105	NGK_2574
	LOS sialylation	lst	NGO1081	NGK_0687
	LOS synthesis	kdtA/waaA	NGO1915	NGK_2338
		lgtA	-	NGK_2630
		lgtB	NGO2156	NGK_2631
		lgtC	XNG2047*	NGK_2632
		lgtD	NGO2158	NGK_2634
		lgtE	NGO2159	NGK_2635
		lgtF	NGO1353	NGK_1584
		lgtG	NGO2072	NGK_2534
		rfaC	NGO1934	NGK_2317
		rfaF	NGO0987	NGK_0802
		rfaK	NGO1354	NGK_1585
	Phosphoethanolamine modification	lptA	-	NGK_1498
	Type IV pili	pilC	NGO0055	NGK_0074; NGK_2342
		pilD	NGO1670	NGK_2057
		pilE	-	NGK_2161; NGK_1796; NGK_2164; NGK_2192; NGK_2167; NGK_1492; NGK_2193; NGK_2191
		pilF	NGO1673	NGK_2060
		pilG	NGO1669	NGK_2056
		pilH	NGO0452	NGK_0623
		pilI	NGO0453	NGK_0624
		pilJ	NGO0454	NGK_0625
		pilK	NGO0455	NGK_0626
		pilM	NGO0098	NGK_0141
		pilN	NGO0097	NGK_0140
		pilO	NGO0096	NGK_0139
		pilP	NGO0095	NGK_0138
		pilQ	NGO0094	NGK_0137

		pilS	-	NGK_0845; NGK_2194; NGK_2578; NGK_2165; NGK_2232; NGK_0104
		pilT2	NGO0346	NGK_0503
		pilT	NGO1908	NGK_2349
		pilU	NGO1909	NGK_2348
		pilV	NGO1441	NGK_1702
		pilW	NGO0595	NGK_1323
		pilX	NGO0456	NGK_0627
		pilZ	NGO0348	NGK_0505
Efflux pump	FarAB	farA	NGO1683	NGK_2072
		farB	NGO1682	NGK_2071
	MtrCDE	mtrC	NGO1365	NGK_1598
		mtrD	NGO1364	NGK_1597
		mtrE	NGO1363	NGK_1596
Immune modulator	Factor H binding protein	fHbp	NGO0033	NGK_0041
	Neisserial surface protein A	nspA	NGO0233	NGK_0365
Invasion	Class 5 outer membrane protein	opc	-	NGK_0937
	Opacity protein	opa	NGO0070; XNG0062*; XNG0952*; XNG1181*; XNG1437*; XNG1948*; NGO1513; XNG0877*; XNG0987*; XNG1352*; XNG1746*	NGK_0693; NGK_1847; NGK_2410; NGK_0749; NGK_1495
	PorA	porA	XNG0832*	NGK_0907
	PorB	porB	NGO1812	NGK_2459
Iron uptake	ABC transporter	fbpA	NGO0217	NGK_0350
		fbpB	NGO0216	NGK_0349
		fbpC	NGO0215	NGK_0348
	Ferric enterobactin transport protein A / ferric-repressed protein B	fetA/frpB	NGO2093	NGK_2557
	Heme uptake	hpuA	XNG2004*	NGK_2581
		hpuB	NGO2109	NGK_2580
	Hemoglobin receptor	hmbR	XNG1216*	NGK_1538
	Lactoferrin-binding protein	lbpA	-	NGK_0401
		lbpB	-	NGK_0400
	Ton system	exbB	NGO1378	NGK_1615
		exbD	NGO1377	NGK_1614
		tonB	NGO1379	NGK_1616

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	Transferrin-binding protein	tbpA	NGO1495	NGK_1771
		tbpB	NGO1496	NGK_1770
Protease	IgA protease	iga	NGO0275	NGK_0419
Stress adaptation	Catalase	katA	NGO1767	NGK_2512
	Manganese transport system	mntA	NGO0170	NGK_0222
		mntB	NGO0169	NGK_0221
		mntC	NGO0168	NGK_0220
	Methionine sulphoxide reductase	msrA/B(pilB)	NGO2059	NGK_2172
	Recombinational repair protein	recN	NGO0318	NGK_0467
Toxin	Neisseria ADP-ribosylating enzyme	narE	NGO0563*	NGK_1361*

Discussion

The results obtained in this research have revealed consistency with both the nature of these bacteria and the reported virulence factors in literature. In the case of N. gonorrhoeae, reported virulence factors in VFDB were in accordance with the literature reports, mostly due to N. gonorrhoeae historically had garnered more attention and seen more extensive research [5]. Indeed, the results revealed well-defined and clearly outlined, also numerous, categorization in both virulence factor classes and factors themselves. This can be clearly attributed to the nature of N. gonorrhoeae since it's primarily an extracellular pathogen with a facultative intracellular phase, therefore its reliance on antigenic variation to better evade immune responses [15]. Also, it should be emphasized here that N. gonorrhoeae has the typical properties of a Gram (-) bacteria that can survive without a host, and has a larger genome together with metabolic independence [5,15] (Auriti et al., 2021, Dubbink et al., 2018). The reliance of N. gonorrhoeae for adherence was due to its dependence on antigenic variation that was extensively reported for Type IV pili [9] and LOS mechanisms [7]. The obtained results were in agreement with the literature as N. gonorrhoeae strains have high amounts of virulence factors related to lots of related genes in both Type IV pili and LOS secretion factors. Genetic diversity in virulence factors and multigenic interactions in virulence factors of N. gonorrhoeae were reported in literature [11]. The high amounts of related genes in various virulence factor classes in N. gonorrhoeae strains, and multiple coding sequences for same virulence factor observed in N. gonorrhoeae NCCP11945 strain support this reporting. Studies about the virulence factors of N. gonorrhoeae primarily focused on Type IV pili and LOS mechanisms since these two were reported to be principally responsible for antigenic mimicry [7,11,15], which was also apparent in the obtained results. Alternative postulations about the virulence factors of N. gonorrhoeae primarily reported for efflux pumps and Iron-transport systems [11], which were also evident in the results due to both Efflux pumps and Iron uptake classes have prominent presence. Noticeable among the results that N. gonorrhoeae FA 1090 strain was missing coding sequences for 7 reported virulence factors, which indicates that genomic variation between strains is possible and requires further research.

As for the C. trachomatis, the reported virulence factor classes in VFDB were quite limited, yet with quite high amounts of factors and related genes. Indeed, despite there were different virulence factors reported in various studies, the results were almost entirely contained Type III Secretion System and it's effectors, which was the most prominently reported and extensively studied virulence factor of C. trachomatis. Among the obtained results, the VFDB were returned no classes for reported virulence factors of plasmid-encoded virulence factors [8,9] and Polymorphic Membrane Proteins [12] despite them being seen extensive research. At this point, the obligate intracellular nature and distinct biphasic life-cycle of C. trachomatis can be reasoned for this result [14]. With a small genome and metabolic dependence to its host, along with its primary modus operandi of hiding and surviving undetected, C. trachomatis becomes a natural manipulator of cellular activities of it's host to facilitate successful infections [10]. Therefore, despite the reporting of numerous virulence factors and postulations of virulence mechanisms for C. trachomatis, it can be said that clear associations of virulence factors still remain a challenge, and this can be attributed to the absence of reported virulence factor classes from VFDB. Since C. trachomatis reported to have increasing infection rates and noticeable difficulty in diagnosis [4], the deficiency in well-defined associations of reported virulence factors with C. trachomatis strains necessitates more detailed molecular research employing multi-omics approaches. This situation can be seen from the absence of related genes for certain virulence factors despite the presence of coding sequences. Nevertheless, strain homogeneity was also observed in C. trachomatis strains, indicating a possible uniform adaptation across strains or lesser reliance on variation.

Conclusions and Future Perspective

C. trachomatis and N. gonorrhoeae infections apparently will remain as serious challenges for public health due to perceived difficulty in diagnosis and increased rates in infections, which also further become compound due to fact of co-infections with these two bacteria. Despite from distant phyla, these two species are known to infect same anatomical sites and develop almost same clinical synopses, albeit utilizing distinct mechanism and having different life-cycles. Apparently, Neisseria species developed highly intricate defensive measures and Chlamydia species developed highly specialized keys for the same end, which bring them together, yet set them apart all the same. Here the necessity of embracing multi-omics-based approaches to address public health challenges becomes evident. Utilization of large-scale genomics studies on strains of these bacteria and making concrete links between gene-to-function scales by association studies are evidently becoming more viable for identification and validation of virulence mechanisms employed by these bacteria, particularly for Chlamydia species. However, it is safe to say that clinical microbiology studies are also required, which should be fed by data from omics research to further develop precise diagnostic approaches and targeted therapy strategies. Finally, results in this research have the potential to direct further studies on C. trachomatis and N. gonorrhoeae for target-based research, particularly on absent factors, factor-related genes, and strain variation.

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Declarations:

Authors' Contribution:

- All Authors Conceptualization, data collection, interpretation, drafting of the manuscript and intellectual revisions
- The authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed

Data Availability Statement

- All data generated or analyzed during this study are included in this published article

Use of Artificial Intelligence Tools

The authors declare that an artificial intelligence (AI) tool was utilized during the control of writing qualifications of this manuscript. Claude (Anthropic) was employed to assist with language editing and scientific writing refinement. All AI-generated content was critically reviewed, verified, and revised by the authors, who assume full responsibility for the accuracy, integrity, and originality of the final manuscript.

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