Journal of Pharmaceutical Research International

33(60B): 1592-1599, 2021; Article no.JPRI.79500
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Pathogenesis and Virulence of Chlamydia Trachomatis

Aastha Parashar [a*] and Mrinangka Deb [b]

[a] Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha, Maharashtra, India.
[b] Department of Microbiology, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi (M), Wardha, Maharashtra, India.

Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i60B34782

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/79500

Review Article

Received 25 October 2021
Accepted 20 December 2021
Published 23 December 2021

ABSTRACT

The pathogenesis of C. trachomatis disease is a multi-step process that includes: (1) infectivity and exposure to the organism (2) Susceptibility to infection and sickness related to the host's genetic makeup. Recurrence and chronic infections are also common in at-risk teenage and young adult groups. Antibiotic resistance to the primary medications used to treat C. trachomatis is becoming increasingly widespread, even with the correct diagnosis. Chlamydial infection can prevent tumor necrosis factor (TNF)-an-induced physiological apoptosis. Failure to adequately prevent, identify, treat, and remove infection increases the risk of pathogenicity and illness. The plasmid glycoproteins 1–8 (pGP1–8) encode eight open reading frames and most Chlamydia species. In the United Kingdom, there has been a recent increase in the prevalence of such illnesses, whereas, in the Scandinavian nations, there has been a drop, albeit there has been a minor increase in recent years (owing to the development of nucleic acid testing technologies, to some extent). However, it should be noted that reliable monitoring systems and population-based data are Chlamydia trachomatis 4 gitis. Chlamydia trachomatis is made plasma or accessible; moreover, it's weakened in the vaginal canal of the mouse and nonhuman primate ocular tissue. The plasmid-free organisms 'in vivo but not in vitro traits were completely mimeographs when pGP3 was inadequate, demonstrating that plasmid-encoded pGP3 is a critical virulence factor in vivo. Moreover, leading to a shortage of cost-effective moment in time tests, including methodologies

**Corresponding author: E-mail: aasthaparashar2000@gmail.com;*

consistent with strain typing during therapeutic, and the overall degree underlying therapeutic failure is foreign. Those disadvantages were exacerbated because the rest of the genders' infestations were undiagnosed, allowing continuous silence propagation and developmental defects. The popular medications C. tachometers are becoming more prevalent with proper identification.

Keywords: Innate along with acquired immunity; Reiter's syndrome; 7.5-kilobyte plasmid; chlamydia murid arum; pGP4; pGP3.

1. INTRODUCTION

Humans are infected with Chlamydia trachomatis, and C. pneumonia, pigs with Chlamydia suis, mice with Chlamydia muridarum, and other species are for colonizing various host species in the Chlamydiaceae family of obligate intracellular bacteria. Guinea pigs and cats are poisoned by Chlamydia caviae and Chlamydia felis, respectively psittaci bacteria-carrying bugs can infect the person's respiratory tract, producing dreadful septicemia. Humans, on other hand, are primarily concerned with Chlamydia trachomatis, a sexually transmitted infection. The genus Chlamydia, it involves Chlamydiaa trachomatiss, Chlamydiaa psittacci, Chllamydia pneumoniaee, along with, Chlamydiaa pecorum is most recent addition too thee Chlamydia subfamily. The homology of DNA between Chlamydial species has been approximated not as much as 10%. Chlamydiaa trachomatous is thee world's majority customary infection transmitted through sexual intercourse (STD).The real prevalence and incidence of this disease are unknown. World Health Organization (WHO) says that every year, almost 100 million new instances of lower genital tract infections are reported, according to them. However the most off females in the company of these infections have no symptoms, hence theey go unobtrusive. According to A systematic review says that according to them, In symptomless women of Europe continent, thee pervasiveness of C. trachomatis fluctuated froom 1.70 too 17.0%. The prevalence of STD among young women who have taken part in clinics for STD is quite higher than 10%, and in studies based on population, the prevalence among under 30-year-olds in the Netherlands, Denmark, and the United Kingdom was in between 2 and 6%. The figure of infections caused by chlamydia in the genital region was recorded and it is on the ascent,though it's indistinct either it iss related too escalated trial otherwise an escalate inn thee number of cases [1].

The cryptic plasmid is detected in maximum clinical isolates and is extensively disseminated among many distinct strains of chlamydia, this fact suggests that the plasmid comes up with advantages for plasmid-rich chlamydial organisms. Furthermore, the homology of the plasmid sequence closely bears a resemblance to that of the genome of chlamydia which implies that the plasmid was chosen for its ability to adapt to a variety of hosts of Chlamydia [2].

During the time of chlamydial infection, all 8 transcripts from plasmids are translated into proteins.In spite of the fact that precise functions of these proteins have yet to be resolved, it is possible that the plasmid is maintained to complete functions which are essential for chlamydial infection advancement. There was no detectable difference in in vitro growth in cultured cells between the pllasmid-inadequate Chlamydia trrachomatis L2 strain acquired fromm inflammation of rectum and colon outpatient and L2 strain of a wild type, which implies that thee pllasmid isn't necessary in favour of maturation of chlamydia ex vivo. A recent study found that a Chlamydia traachomatis urethra isolate (aa serovarr B variation) could be cultivated and recovered successfully without the plasmid aided this conclusion. Trachma, lymphogranuuloma venereumm, along with murinne pneumoniitis emissary, these are the three biovariants (biovars) of C.trachomatis. Homology of the DNA analyses the three C. trachomatis, as well as direct comparisons of sequences of DNA off determined nucleic acids, experienced let fall in such a manner that the trachomma and lymphogranuloma venereum (LGV) group of micro organisms are almost equivalent,the murine biovar, on the other hand, is more distantly connected [3].

1.1 Objective

Review of Chlamydia trachomatis pathogenesis and virulence.

1.2 Biology of Chlamydia

A chlamydial infection can cause the development of proinflammatory cytokines, as well as an immunological response to the agent and antibodies to heat shock proteins (hsp). For example, to hsp60 (Witkin et al. 1996). Chlamydia is a sexually transmitted disease.It has been discovered that human hsps and other bacteria share epitopes.It's been suggested that chlamydial infections could cause elicit an immunological reaction The manufacture of hsp60 is possible,produce localised inflammatory reactions, such as in the gastrointestinal tract RBs may be able to evade the immune reaction by passing through the uterine tubes.As a result, persistent infections can be explained. the creation of new EBs derived from RBs can elicit an immunological response. Inflammatory responses that lead to a cyclic phase of the diseased tissue is scarred. This is an example.The elementary body (EB) is extracellular, and is an transmissible form which is characterized by an osmotically resistant outer membrane and a highly condensed chromosome [4].

The reticulate body (RB) is a chlamydiae replicative intracellular form. Chlamydiae are classified as energy parasites because they are unable to generate a net gain of ATP and hence rely on the host for energy. Because of this, Chlamydia's cell-free development has been abandoned, and in vitro growth requires the use of cell culture methods or yolk sacs. The envelope strangle is another distinguishing feature of Chlamydiae [5].

1.3 Developmental Cycle of Chlamydia

Several ligands of bacterial and host receptors are involved in engaging to the host cell16–18 (Fig. 1). When T3SS effectors come in proximity with the elementary body, the elementary body is internalised into the inclusion. Early genes are translated and the shift to the reticulate body takes only a few hours (6–8 hours post-infection for C. trachomatis). The term "nongonoccocal urethritis" (NGU) was coined to describe urethral discharge that was not caused by gonorrhoea (Dunlop et al. 1972). The true aetiology of these cases was uncovered after procedures to diagnosis C. trachomatis infection were established. NGU cases exceeded gonococcal urethritis cases by the end of the 1970s, a trend that has continued in most nations. This is also true for urethritis that remains after gonorrhoea has been cured microbiologically but not clinically, i.e. postgonococcal urethritis (PGU). PGU is frequently caused by a C. trachomatis infection that has not responded to traditional gonorrhoea treatment. Exocytic vesicles are guided to the inclusion, and host–pathogen interactivities are ameliorated [6].

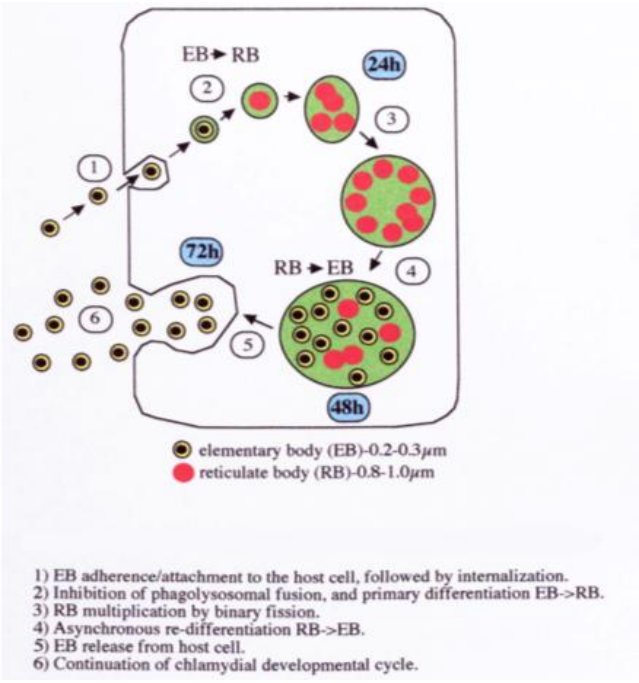

Fig. 1. Schematic representation of the Chlamydial development cycle

Genes of mid-cycle are then subsequently produced (8–16 hours after C. trachomatis infection) and hold effectors that arbitrate nutrition for the survival of the host. The bacteria carves up via binary fission, which gives rise to the inclusion to grow remarkably. Individual inclusions are generated when many elementary bodies contaminate a single cell in some species, such as C. trachomatis, and they homotypically put together with each othered. During this stage, some late-cycle receptors are bundled in progeny elementary bodies, ready to be allowed to leave during the successive infection cycle.Toxic factors of chlamydia in governing the morbific consequence of chlamydial infection in the catarrhine female genital tract representation [7].

1.4 Implementation of Attachment and Entry

When the elementary body (EB) of chlamydial gets into deal with the epithelial cell membrane of the anchor, the infectious operation starts. The recognition of adhesins (i.e. the predictor of initial elementary body (EB /cell interconnections)of chlamydia is not studied, but a number of acknowledged adhesins have been put further, as well as the outer membrane protein (MOMP)of chlamydia,chlamydial cytadhesin (CCA), a heparan sulphate-like glycosaminoglycan (GAG), and chlamydial heat shock protein (CH).Inspite of the fact that the precise technique of elementary body (EB) engrossment is not calculated, conjectures consist of receptor-mediated endocytosis in trenches carpeted with clathrin, pinocytosis in non-carpeted trenches, and bloodsucker-specific internalization [8].

1.5 Multiplication and Growth

Because of the early start, production of proteins of chlamydia, the chlamydiae remain within an inclusion that does not merge with lysosomes once they have entered the host cell. The fundamental divergence of elementary body (EB) to reticulate body (RB) calls for the diminutive splitting of MOMP and supplementary proteins of outer membrane, as well as the unfastening of the nucleic acid of chlamydia. Sphingomyelin is carried to the inclusion membrane originating at the trans-Golgi network of the host, and it has even been found in chlamydiae. Proteins of Chlamydia are thrusted into the inclusion membrane. It appears that the inclusion membrane should be remodelled in chlamydia. Reticulate body(RB) replicates within the inclusion by binary fission, accompanied by the offspring still alive intimately linked until later along with the cytoplasmic insertion layer in the embryonic revolution, implying that sort of close contact is essential for intracellular growth [9].

1.6 Ejection from the Host Cell

The RB to EB differentiation pathway starts asynchronously. 48-72 hours after infection. The detachment of RB from the inclusion membrane has been suggested as a signal for differentiation [10].

1.7 Antigens of Chlamydia

1.7.1 Proteins high in cysteine

The proteins OMP2 and OMP3 are cysteine-rich. found solely in elementary bodies that are specific to developmental stages. MOMP, OMP2, and OMP3 are thought to be substantially di-sulfide cross-linked, mediating the chlamydial elementary body's structural and osmotic resilience. OMP2 has different pI values than the trachoma biovars, which is single enzymatic distinction between , lymphogranuloma venereum (LGV) and the biovars of trachoma [11].

1.7.2 Heat shock proteins

Proteins that are activated by heat. When C. trachomatis-poisoned cells are cultured, exposed to warmth, stress. During the in vitro chlamydial developmental cycle, the pair cHSP60 together with cHSP70 stay contained within the inclusion [12].

1.8 Glycoprotein

LPS (lipopolysaccharide polysaccharide) of chlamydia is an antigen which is group specific. that should be demonstrated to have a 3-deoxy-2-keto sugar that is comparable, 3-deoxy-octulosonic acid is similar, but not identical (Kdo)as an immunodominant group. The two terminal chlamydial Kdo units are joined by a unique 2.8 linkage (coded by the gseA gene), forming a chlamydial distinctive epitope. According to research, chlamydiae produce both a smooth and a rough LPS version [13].

The outer membrane compound of chlamydia of elementary bodies is manufactured of about 60% major protein of outermembrane(MOMP). Major

protein of outermembrane (ompl),a single-copy gene that was originally ordered from LGV2 and comprised of 1,182-bp which encodes 394 albuminoid.[14]

1.9 Pathogenicity

pGP4's Role in Chlamydial Pathogenicity

The discovery came up with the molecular foundation for the Caldwell group's early conclusion that the Chlamydia trachomatis plasmid DNA is a transcriptional selector.When the chromosome outlines of plasmid-free L2R life forms supplemented with the out-and-out plasmid as opposed to a plasmid diminished of pgp4 were compared, pgp3 impression shrinked by four folds, while 9 chromosomal nucleic acids, together with glgA, declined by two to twenty-three folds together with 5 supplementary chromosomal genes escalated by two folds in non-attendance of pgp4. In addition, plasmid-deficient creatures' chromosomal gene expression trended in the same direction as pgp4 striked-out life forms , implying that pGP4 is substantially in the wrong for plasmid-arbitrated gene control.[15]

1.10 Immune Defence Mechanisms

1.10.1 Innate reaction

It is only recently that the significance of the host's reaction to chlamydial infection has been examined. In acute chlamydial infection, an early entrance of white blood corpuscles (perhaps controlled by CD 18, convoluted in lipopolysaccharide binding) was shown to have a substantial role in reducing early illness phases.[16]

The action of pro-inflammatory cytokines could be another simplication for the intrusion of white blood corpuscles to the infection area. The production of pro-inflammatory cytokines may have a role in recruitment of whit blood cells and other corpuscles of inflammation to infection area preliminary to lymphocytes arrive.Persistent stimulation of epithelial cells following re-infection or the commencement of an immune response may increase the local inflammatory response, and IFN-y has been hypothesised to have such an effect during recurrent infections. IFN-y has been found to stimulate the synthesis and secretion of IL-8 in chlamydial infected epithelial cell lines. As a result, greater inflammation may be caused by the synthesis of IFN-, y as part of a Th 1 response. In spontaneous infection, such an increased cytokine response has been observed.[17]

1.10.2 Humoral reaction

According to studies, antibodies aid in protection against C. trachomatis MOMP in mouse models, but they aren't essential. In vitro, however, antibodies have been demonstrated to neutralise C. trachomatis infection. In the presence and absence of complement, neutralisation occurs by either blocking the attachment of chlamydial elementary bodies to the cell or allowing chlamydial internalisation but inhibiting/preventing multiplication. Lymphocytic proliferation experiments revealed that humans produce cell-mediated immune responses to chlamydial genital tract infection. According to animal and human research, the protective response against chlamydial infection is predominantly T hl related. People who have a poor cell-mediated immune system. Immune responses and powerful antibody responses have been demonstrated to be susceptible to reinfection, slow to heal infection, and have significant levels of clinical inflammation and sickness in scarring disease [18].

Non-gonococcal bacteria causing Urethritis.

Non-gonococcal urethritis (NGU) is urethritis that is caused by a bacteria other than Neisseria gonorrhoeae. C. trachomatis has been detected in the urethral samples of close to 13 percent to 50 percent of NGU patients, with the remaining cases attributed to Trichomonas vaginalis, Herpes simplex virus, and Mycoplasma genitalium. There is no variation in clinical outcomes among chlamydial and non-chlamydial NGU.[19]

1.10.3 Venereal lymphogranuloma

Lymphocytic granuloma venereum (LGV) is a systemic, transmissible disorders which we get through sexual contact are caused by C. trachomatiss erovars L 1 to L3. The countries of East and West Africa, India, Southeast Asia, and South America are all affected. LGV causes an ulcer that appears 3–12 days after infection and affects the coronal, suculus, inner foreskin, or glans penis in male and the rear vaginal wall, fourchette, or posterior cervical line in females [20].

1.11 Diagnosis in Lab

1.11.1 Specimens

As we know Chlamydia is an intracellular organism, the most vital goal is that the specimen should obtain from host cells that contain the microorganism. A well designed media is used for the collection of specimen, such as 0.2Molarity sucrose in phosphate buffered saline (2SP) [21].

Method used for the preservation of tissue is known as Tissue culture. Many scientists worked on it and used different technique for tissue culture for example –Gordon used irradiated McCoy cells to demonstrate and distinguish the first cell culture for C. trachomatis in vitro growth. Immunizing or Inoculating patient specimens onto cell monolayers is how culture is done. While the technique has a high particularity and explicitness of 100 percent, it has a lesser sensitivity (70-85 percent) than DNA amplification techniques. There are few of the cell lines such as BGMK and McCoy cells that have been used to propagate C. trachomatis. A high frequency sound waves sonicate the bacterial celles to destroy cellular components and free chlamydial elementary bodies are done prior to the cultivation or development [22].

2. CONCLUSION

COVID is pandemic situation in whole world which goes through trouble and due to these condition economic status of most of the countries is decreses due to lockdown\ shutdown in economically stable countries . Wuhan in china is origin of COVID – 19 pandemic , death rate of COVID patient is gradually increases due to incomplete availability of hospitalization ,and deacreses in oxygen supply in hospital, COVID patient follows the symptoms like coughing, pneumonia, double pneumonia, chest pain, low oxygen supply to patient suffering from covid situation ,dosage vaccine and amount of availability of vaccine controls the situation (patients health, and economic control . KOH technique is expensive screening test. Candida is often cause fungal infection. Overgrowth of fungi can result from drug overuse which can harm basic vaginal enviornment, loss of immune system [23].

Among the eight pGPs identified by chlamydial plasmids, only pGP3 is both localised in the outer membrane complex and liberated into the cytoplasm of the host cell. Medical negligence (carelessness , non performance ,laxness) is at peak to concern about pubic health among public health care provider as it effect public health and safety and also not only helth also wealth . Or any dis ability which Is permanent to subject or patient .the patient safety is depend on doctors skill and experience that how he \she is gone treat the subject. Because Chlamydia can finish its manufacture inside an inclusion, the chlamydial proteins it produces can interact with host cells. The immunodominant pGP3 protein has been linked to illnesses in infected patients. Due to its C-terminal trimerization dominion (pGP3c), which is comparable to TNF's receptor binding dominion, it is a well-constructed trimer [24-29].

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Everett KD, et al. Emended description of the order Chlamydiales, proposal of Parachlamydiaceae fam. nov. and Simkaniaceae fam. nov., each containing one monotypic genus, revised taxonomy of the family Chlamydiaceae, including a new genus and five new species, and standards for the identification of organisms. Int J Syst Bacteriol. 1999;49(Pt 2):415–440. [PubMed] [Google Scholar]
2. Budrys NM, et al. Chlamydia trachomatis antigens recognized in women with tubal factor infertility, normal fertility, and acute infection. Obstet Gynecol. 2012;119:1009–1016. [PMC free article] [PubMed] [Google Scholar]
3. Lovett M, et al. Plasmids of the genus Chlamydia. In: Nelson J, Grassi C, editors. Current chemotherapy and infectious diseases. American Society Of Microbiology; 1980.
Published by.
[Google Scholar]

4. Thomas NS, et al. Plasmid diversity in Chlamydia. Microbiology. 1997;143(Pt 6):1847–1854. [PubMed] [Google Scholar]
5. Carlson JH, et al. Comparative genomic analysis of Chlamydia trachomatis oculotropic and genitotropic strains. Infect Immun. 2005;73:6407–6418. [PMC free article] [PubMed] [Google Scholar]
6. Sriprakash KS, Macavoy ES. Characterization and sequence of a plasmid from the trachoma biovar of Chlamydia trachomatis. Plasmid. 1987;18:205–214. [PubMed] [Google Scholar] .
7. Comanducci M, et al. Diversity of the Chlamydia trachomatis common plasmid in biovars with different pathogenicity. Plasmid. 1990;23:149–154. [PubMed] [Google Scholar]
8. Seth-Smith HM, et al. Co-evolution of genomes and plasmids within Chlamydia trachomatis and the emergence in Sweden of a new variant strain. BMC Genomics. 2009;10:239. [PMC free article] [PubMed] [Google Scholar]
9. Hatt C, et al. Analysis of the entire nucleotide sequence of the cryptic plasmid of Chlamydia trachomatis serovar L1. Evidence for involvement in DNA replication. Nucleic Acids Res. 1988;16:4053–4067. [PMC free article] [PubMed] [Google Scholar]
10. Comanducci M, et al. The structure of a plasmid of Chlamydia trachomatis believed to be required for growth within mammalian cells. Mol Microbiol. 1988;2:531–538. [PubMed] [Google Scholar]
11. Romanchuk KG. Fluorescein. Physicochemical factors affecting its fluorescence. Survey of ophthalmology. 1982 Mar 1;26(5):269-83.
12. Lanjouw E, Ouburg S, De Vries HJ, Stary A, Radcliffe K, Unemo M. 2015 European guideline on the management of Chlamydia trachomatis infections. International journal of STD & AIDS. 2016 Apr;27(5):333-48.
13. Carlson JH, Porcella SF, McClarty G, Caldwell HD. Comparative genomic analysis of Chlamydia trachomatis oculotropic and genitotropic strains. Infection and immunity. 2005 Oct;73(10):6407-18.
14. Ryan Jr GM, Abdella TN, McNeeley SG, Baselski VS, Drummond DE. Chlamydia trachomatis infection in pregnancy and effect of treatment on outcome. American journal of obstetrics and gynecology. 1990 Jan 1;162(1):34-9.
15. Gaydos CA, Howell MR, Pare B, Clark KL, Ellis DA, Hendrix RM, Gaydos JC, McKee Jr KT, Quinn TC. Chlamydia trachomatis infections in female military recruits. New England Journal of Medicine. 1998 ;339(11):739-44.
16. Papp JR, Schachter J, Gaydos CA, Van Der Pol B. Recommendations for the laboratory-based detection of Chlamydia trachomatis and Neisseria gonorrhoeae—2014. MMWR. Recommendations and reports: Morbidity and mortality weekly report. Recommendations and reports/Centers for Disease Control. 2014 Mar 14;63:1.
17. Mårdh PA, Ripa T, Svensson L, Weström L. Chlamydia trachomatis infection in patients with acute salpingitis. New England Journal of Medicine. 1977 Jun 16;296(24):1377-9.
18. Molano M, Meijer CJ, Weiderpass E, Arslan A, Posso H, Franceschi S, Ronderos M, Munoz N, Van Den Brule AJ. The natural course of Chlamydia trachomatis infection in asymptomatic Colombian women: a 5-year follow-up study. The Journal of infectious diseases. 2005 Mar 15;191(6): 907-16.
19. Nicholson TL, Olinger L, Chong K, Schoolnik G, Stephens RS. Global stage-specific gene regulation during the developmental cycle of Chlamydia trachomatis. Journal of bacteriology. 2003 May 15;185(10):3179-89.
20. Müller-Schoop JW, Wang SP, Munzinger J, Schläpfer HU, Knoblauch M, Tammann RW. Chlamydia trachomatis as possible cause of peritonitis and perihepatitis in young women. Br Med J. 1978 Apr 22;1(6119):1022-4.
21. Brunham RC, Rappuoli R. Chlamydia trachomatis control requires a vaccine. Vaccine. 2013 Apr 8;31(15):1892-7.
22. Grimwood J, Stephens RS. Computational analysis of the polymorphic membrane protein superfamily of Chlamydia trachomatis and Chlamydia pneumoniae. Microbial & comparative genomics. 1999;4(3):187-201.
23. Harrison HR, Alexander ER, Weinstein L, Lewis M, Nash M, Sim DA. Cervical Chlamydia trachomatis and mycoplasmal infections in pregnancy: epidemiology and

outcomes. Jama. 1983 Oct 7;250(13): 1721-7.

24. Mpiga P, Ravaoarinoro M. Chlamydia trachomatis persistence: an update. Microbiological research. 2006 Jan 1;161(1):9-19.
25. Dasari, Venkatesh, and Kiran Dasari. Nutraceuticals to Support Immunity: COVID-19 Pandemic- A Wake-up Call. Journal of Clinical and Diagnostic Research. 2020;14(7):OE05–9. Avaialble:https://doi.org/10.7860/JCDR/2020/44898.13843.
26. Dhok, Archana, Lata Kanyal Butola, Ashish Anjankar, Amol Datta Rao Shinde, Prakash Kesharao Kute, and Roshan Kumar Jha. Role of Vitamins and Minerals in Improving Immunity during Covid-19 Pandemic - A Review. Journal of Evolution of Medical and Dental Sciences-JEMDS. 2020;9(32):2296–2300. Avaialble:https://doi.org/10.14260/jemds/2020/497.
27. Vagga AA, Butola LK, Khadhe SG, Meshram KA. Association of Natural Antioxidants and Immunity in Covid-19 Pandemic. Journal of Evolution of Medical and Dental Sciences-JEMDS. 2021 Mar 1;10(9):613–8.
28. Abbafati, Cristiana, Kaja M. Abbas, Mohammad Abbasi, Mitra Abbasifard, Mohsen Abbasi-Kangevari, Hedayat Abbastabar, Foad Abd-Allah, et al. Five Insights from the Global Burden of Disease Study 2019. LANCET. 2020;396(10258):1135–59.
29. Abbafati, Cristiana, Kaja M. Abbas, Mohammad Abbasi, Mitra Abbasifard, Mohsen Abbasi-Kangevari, Hedayat Abbastabar, Foad Abd-Allah, et al. Global Burden of 369 Diseases and Injuries in 204 Countries and Territories, 1990-2019: A Systematic Analysis for the Global Burden of Disease Study 2019. LANCET. 2020;396(10258):1204–22.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/79500