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Research Article

Observable Variations in Serum Toll Like Receptors (TLR4) As an Adjunct for Detection of Asymptomatic *Neisseria gonorrhoea* Infection Amongst Sexually Active Women in Osun state, Nigeria

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Abstract

Background of Study: The genus Neisseria contains commensal and pathogenicspecies that colonize human mucosal epithelia. The pathogenic species *Neisseria gonorrhoeae* and *Neisseria meningitidis* can induce inflammation and breach mucosal barriers. they have evolved mechanisms to promote growth and persistence in the host. In addition to living freely in the extracellular space, *N. gonorrhoeae* can invade the cytoplasm of host phagocytes, thereby evading detection and elimination by the innate immune system.

Aim and Objectives: To evaluate molecules from microorganisms known as pathogen-associated molecular patterns through which several host pattern recognition receptors are mediated as an adjunct for early detection of Asymptomatic carriers from symptomatic carriers these molecules is the Toll-like receptors (TLRs). For example, TLR4mediates recognition of extracellular gonococcal lipoolextracecharide (LOS).

Materials and Method: Adult sexually active females those who haven't been diagnosed of any sexually transmitted infection and then positive carriers those who have been diagnosed and confirmed with N. Gonorrhea infection using the normal healthy females as a baseline of comparison from both. Blood samples where collected, 10 positive Symptomatic carriers and 10 Asymptomatic carriers were inducted into this study all patient on any form of antibacterial treatment were excluded from the study. Veinus blood samples where collected and analysed with the flow cytometer to differentiate TLR4 Neutrophils and Monocytes with other proinflammatory mediators.

Result: Observable variations when comparing the normal healthy female and the asymptomatic carrier with a significant differences ($p < 0.05$) from the TLR4 (Neutrophils and Monocytes) although symptoms may not be present but the body still produces mediators as baseline of infectious antigen present.

Conclusion and Recommendation: It is possible to include TLR4 as mediator in detecting possible sexually transmitted gonococcal infection in females.

Keywords: Toll like Receptors; Mediators; Immunostimulation; Gonococcal; Asymptomatic

Introduction

The detection of pathogens happens through the common mediator molecules from microorganisms known as pathogen-associated molecular patterns (PAMP) through several host pattern recognition receptors including Toll-like receptors (TLRs). For example, TLR4 mediates recognition of extracellular gonococcal lipooligosaccharide (LOS) [9]. It has additionally been proven that lipopolysaccharide (LPS) and infection with distinctive gram negative and gram positive bacteria induces interferon (IFN)-b [7].

The genus Neisseria incorporates commensal and pathogenic species that colonize human mucosal epithelia. The pathogenic species Neisseria gonorrhoeae and Neisseria meningitidis can induce irritation and breach mucosal barriers. Each year *N. Gonorrhoeae* and *N. Meningitidis* purpose an envisioned 88 million cases of gonorrhea and 500,000 cases of meningococcal meningitis worldwide, respectively. These pathogens are tremendously tailored to humans; in preference to produce cytotoxins or secrete poisonous products, they have advanced mechanisms to promote increase and persistence within the host. In addition to dwelling freely inside the extracellular space, *N. Gonorrhoeae* can invade the cytoplasm of host phagocytes, thereby evading detection and removal via the innate immune system [1,2].

The sensing of pathogen-derived nucleic acids (DNA and RNA) is a central approach used by the innate immune system to initiate immune responses following microbial invasion. Accumulation of overseas or self-DNA inside the cytosol can result in robust innate immune responses through a lot of sensors. An endoplasmic-retic-

ulum resident host protein called stimulator of IFN genes (STING) is required for a type I IFN response to cytosolic double-stranded DNA (dsDNA) [3], and IFN responses to a own family of specific bacterial nucleic acids that shape cyclic dinucleotides [10]. STING has been shown to have vital roles within the innate immune responses to many bacterial pathogens [5,8]. Recent research have stated that the enzyme cyclic GMPAMP synthase (cGAS) acts as an intracellular DNA sensor for cytosolic DNA, generating the second messenger cGAMP. CGAMP binds to STING and leads to IRF3 phosphorylation and kind I IFN production [10-12].

Materials and Methods

A total of 10 Asymptomatic Culture confirmed cases of Neisseria gonorrhoea infection in 10 sexually active females where identified, a few of them by their sexual male counterpart who experienced symptoms. Venous blood was collected from the asymptomatic confirmed females and the symptomatic confirmed females, the samples was analysed using a flowcytometry, with the forward, sideways and backwards scatter of light calculating the various parts of the Toll like receptors and the inflammatory mediators like the IL (interleukin).

Results

From the result, there was observable elevation of Toll like receptor 4, which serves as a protective mechanism against the LOS of *N. gonorrhea* and the body response through the mediation of Chemokines and recognition by the PAMPS, pathogen associated molecular patterns, the symptomatic females had and elevated TLR4 and inflammatory mediators which is significant ($P < 0.05$) when compared to the uninfected female control groups and the asymptomatic group. For control TLR4 Neutrophil (428.8 ± 12.18, 678.0 ± 13.29 and 495.3 ± 16.64) and TLR4 monocyte (1069 ± 37.86, 1591 ± 47.45 and 1347 ± 60.5) as seen in Table 1.

	Control (n = 10)	Symptomatic (n = 10)	Asymptomatic (n = 10)	P. value
TLR4 (neutrophil) (AFU)	428.3 ± 12.18	678.0 ± 13.29	495.5 ± 14.64	0.0001
TLR4 (Mononcytes) (AFU	1069 ± 37.86	1591 ± 47.45	1347 ± 60.5	0.0001
IL-ß1 pg/ml	60.8 ± 1.21	128.7 ± 2.59	110.9 ± 2.50	0.0001
IL-16 pg/ml	67.0 ± 1.70	116.1 ± 1.50	101.0 ± 1.73	0.0001
TNF pg/ml	33.5 ± 0.94	93.20 ± 1.13	78.8 ± 1.86	0.0001

Table 1: Comparative analysis of TLR4 levels in Symptomatic and Asymptomatic carriers of *Neisseira gonorrhoea.*

Key: TLR4: Toll Like Receptor; IL-ß1: Interleukin 1, a Chemokine; IL-6: Chemokine; TNF: Tumour Necrosis Factor, All Inflammatory Mediators.

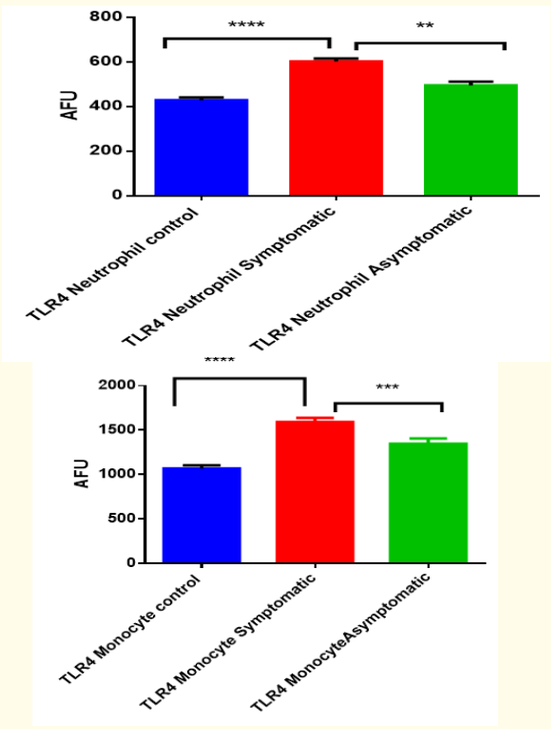

Figure 1: Comparative Levels of TLR4 Neutrophil and Monocyte in Asymptonmatic and Symptomatic *N. gonorrhea* Infection in Sexually active females.

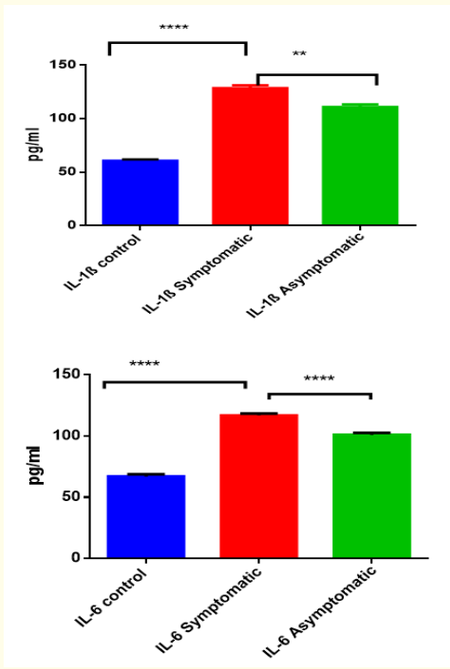

Figure 2: Comparative Levels of the inflammatory mediators Interleukin (IL-ß1 and IL-6) in Asymptonmatic and Symptomatic *N. gonorrhea* Infection in Sexually active females.

Discussion

TLR4 neutrophils

The TLR4 neutrophil showed a significant increase in the asymptomatic females when compared with the control group 495.5 ± 16.4 and 428.3 ± 12.18 ($P < 0.05$) this shows that there is a significant increase although this increase may not yield to symptoms to it keeps it in check and controlled although there is more attributed to asymptomatic females who seem to be carriers of gonorrhoea with most or all of their male counterparts exhibiting symptoms associated with clap during infectious incubation of the pathogen as compared with other studies with female mice and increased TLR4 and TLr2 in mucosa lining of the cervix [4,6].

TLR4 monocytes

The TLR4 neutrophil showed a significant increase in the asymptomatic females when compared with the control group 1069 ± 37.86 and 1347 ± 60.5 ($P < 0.05$) this shows that there is a significant increase although this increase may not yield to symptoms to it keeps it in check and controlled although there is more attributed to asymptomatic females who seem to be carriers of gonorrhoea with most or all of their male counterparts exhibiting symptoms associated with clap during infectious incubation of the pathogen as compared with other studies with female mice and increased TLR4 and TLr2 in mucosa lining of the cervix [4,6].

Inflammatory mediators

There was also observable increase in the inflammatory mediatiors obviously acting as chemokines to recruit TLR4 Monocytes and Neutrophils that in turn act as protective phagocytes either through the complement pathway or by presenting cells to the TH1 cells which in turn activate the complement pathway for the lysis (death) of the pathogen. All these inflammatory markers or mediators thus yield to presentation of symptoms as observable in the males as clap.

Conclusion

The TLR4 and TLR2 both serve as protective mechanism in response to PAMPS, but the TLR4 elevation can be used both as preventive mechanism in immunostimulation as seen in Vaccine or as a determinant for the identification of *N. gonorrhea* in asymptomatic females. Although more study should be done to identify more inflammatory markers triggered by the PAMPs of *N. gonorrhoea.*

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Conflict of Interest

There were no conflict of interest during and after this work.

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