



## Review Article

# Microbial imbalance in Maternal Women A Cause of Neonatal Premature Birth: A Review

Rabiu M<sup>1</sup>, Abdulkadir B<sup>2</sup>, Hayatudeen M<sup>3</sup>, Bello A M<sup>4</sup>, Abidemi O<sup>5</sup>, Kaware M.S<sup>6</sup>,  
Abdullahi B<sup>7</sup>, Tukur A.D<sup>8</sup>, Abdullahi S<sup>9</sup>, Kumurya A. S<sup>10</sup>

1. Department of Medical Laboratory Services Ahmad Sani Yariman Bakura Specialist Hospital Gusau Zamfara State, Nigeria, Department of Medical Laboratory Science, Faculty of Allied Health Sciences, Bayero University, Kano, Nigeria, Department of Public Health Emergency Operations Service Ministry of Health Zamfara State. [generalmurtala@yahoo.com](mailto:generalmurtala@yahoo.com)
2. Department of Microbiology Umaru Musa Yaradua University Katsina State, Nigeria [bashir.abdulkadir@umyu.edu.ng](mailto:bashir.abdulkadir@umyu.edu.ng)
3. Department of Microbiology Ahmadu Bello University Zaria, Kaduna State, Nigeria [hayatudeen.muhammad@umyu.edu.ng](mailto:hayatudeen.muhammad@umyu.edu.ng)
4. Department of Obstetrics and Gyneacology Federal Medical Centre Gusau Zamfara State, Nigeria [Balhaji364@gmail.com](mailto:Balhaji364@gmail.com)
5. Department of Obstetrics and Gyneacology Ahmad Sani Yariman Bakura Specialist Hospital Gusau Zamfara State, Nigeria, [abidemioya@yahoo.com](mailto:abidemioya@yahoo.com)
6. Department of Community Medicine, Umaru Musa Yaradua University Katsina State, Nigeria [musa.kaware@umyu.edu.ng](mailto:musa.kaware@umyu.edu.ng)
7. Department of Microbiology Ahmadu Bello University Zaria, Kaduna State, Nigeria [abuuismael@gmail.com](mailto:abuuismael@gmail.com)
8. Northwest Zonal TB Reference Laboratory, Aminu Kano Teaching Hospital Kano, Kano State, Nigeria, [abubakartukur@gmail.com](mailto:abubakartukur@gmail.com)
9. Department of Clinical Pharmacology, Faculty of Medicine, Umaru Musa Yaradua University Katsina State, Nigeria [albishir13@yahoo.com](mailto:albishir13@yahoo.com)
10. Department of Medical Laboratory Science, Faculty of Allied Health Sciences, Bayero University, Kano State, Nigeria, [askumurya.med@buk.edu.ng](mailto:askumurya.med@buk.edu.ng)

## ABSTRACT

**Background:** A microbiota is a natural network of commensal, advantageous microorganisms found in every multicellular creature. These microorganisms have been found for hormonal, immunologic and metabolic homeostasis of their host. Premature labour has been highlighted as among the significant predicaments in pregnancy and falling in as a significant reason for neonatal morbidity and mortality.

**Aim and Objective:** The aim of this paper is to bring about the present pattern and feature the effect of maternal microbiota and variables related with unexpected labour among pregnant women who along these lines had an unconstrained preterm delivery. **Materials and Method:** Involved a broad search of both electronic literatures by studying and comparing the information obtained from recently published scientific researches in peer reviewed journals, books, and conferences

**Result:** Some of the evaluated writing indicated that *Trichomonas vaginalis* which has been connected with a little danger of preterm delivery and low birth weight and the malady might be secure perinatally and happen in about 5% of children conceived by infected mother, while significant proof shows that Bacterial vaginosis in pregnancy is related with preterm delivery and other unfriendly outcome.

**Conclusion:** the microbiota can cause harm to women and leading to premature delivery in preterm mothers and can also serve as beneficiary normal flora to women vaginal by inhibiting the growth of unwanted microorganisms while some microbiota can also be taken as probiotics medicine or nutrient to provide nourishment to human especially preterm mothers.

**Keywords:** Delivery, Microbiota, Premature, Pregnancy and Vagina

### Corresponding Author:

Rabiu M  
Address: Department of  
Medical Laboratory Services  
Ahmad Sani Yariman  
Bakura Specialist Hospital  
Gusau Zamfara State,  
Nigeria  
Phone No. +2348060652379  
Email:  
[generalmurtala@yahoo.com](mailto:generalmurtala@yahoo.com)

## INTRODUCTION

Untimely labour is one of the principal inconveniences in pregnancy and a significant reason for neonatal morbidity and mortality. It is described by the unconstrained beginning of labour before 37 entire long stretches of gestation<sup>1-2</sup> and confirm by constant uterine constrictions, cervical destruction more prominent than or equivalent to 80% and cervical enlargement more noteworthy than or equivalent to one centimetre<sup>3,4</sup>. Be that as it may, conclusion is frequently overwhelming because of many related elements<sup>3-4</sup>. One hazard factor of untimely labour recognized in the literature is young pregnancy, although there are likewise disputable outcomes.<sup>4-5</sup> It is realized that specific viewpoints identified with way of life and human services, just as others identified with social, segment and wellbeing profiles, can impact these discoveries, although the proof is inadequate in regard to which of these angles identified with high school pregnancies may prompt untimely labour. This brings up issues about the absence of logical data right now infections are regularly constant and normally asymptomatic until labour starts. A more profound comprehension of the connection between intrauterine diseases and preterm delivery will allow the clinical examination of medicines to diminish unconstrained preterm delivery and its related long-term morbidity and mortality<sup>6</sup>. The point of this paper is to look at the present pattern and feature the effect of vaginal microbiota and components related with unexpected labour among pregnant women as this will make ready for handling the issue.

## METHODOLOGY

For this paper the technique utilized was by carefully examining and looking at the data got from current published scientific researchers in peer reviewed journals, books, and conferences.

### Preterm birth

Preterm birth has been characterized as any birth before 37 weeks of finished a long time of gestation<sup>7</sup>. An estimation of 15 million babies is conceived preterm every year with coming about complications<sup>[8]</sup> Preterm birth is a guideline reason for an expected 1 million neonatal deaths yearly and a huge supporter of youth morbidities. The World Health Organization characterizes preterm birth as any birth before 37 weeks of

finished incubation or less than 259 days since the primary day of the lady last menstrual period and it is additionally subdivided into 3 Incredibly preterm:< 28 weeks, very preterm:28-<32 weeks, moderate or late preterm:32 - <37 weeks

### Trend of History in Preterm Birth

Over 60% of preterm births happen in Africa and South Asia. Nations with most noteworthy quantities of preterm births incorporate Brazil, India, Nigeria, United States of America, Pakistan, China, Philippines, Indonesia, and Democratic Republic of Congo<sup>9</sup>. Of the considerable number of nations with preterm birth rates over 15%, everything except two are in sub-Saharan Africa<sup>9</sup>. In least fortunate nations, on normal 12% of infants are brought into the world too early contrasted and 9% in the higher-salary nations and more unfortunate families are at higher hazard, instances of preterm birth have been accounted for in certain nations in Africa; Ethiopia, Ghana and Gambia which all indicated high commonness of preterm births Gambia detailed a high predominance of 10.9% preterm birth rate<sup>10</sup> Comparable examinations have been led in certain states in Nigeria; Niger Delta, Abuja and Kano. Out of 634 deliveries at extraordinary consideration child unit of Niger Delta University Teaching Hospital, 152 (24.0%) were preterm. 132 (90.8%) of the preterm had gestational age during childbirth 24-36 weeks and most were conceived between 28-36 weeks. 69(50%) of preterm babies were from lower class, 25 (18.1%) centre social class and 2 (1.4%) from upper social class<sup>30</sup>. The investigation directed at Aminu Kano showing medical clinic Kano between June 2006-May 2007 detailed 148 preterm births out of 2154 births. 132(89.2%) of preterm births have a place with lower class and 16 (10.8%) were from high society<sup>11</sup>.

### Aetiology and Pathogenesis of Premature Delivery

Preterm delivery isn't uniformly circulated among women. The clearest uniqueness is that the pace of preterm delivery among black women is twice that of any racial gathering of women in the United States with a much more prominent disparity in the pace of early preterm delivery. These distinctions are unexplained anyway progressively dark women have bacterial vaginosis<sup>6</sup>. The recurrence of preterm births is about 12%-13% in the USA and 5-9% in numerous other created

nations anyway the pace of preterm births and delivery of falsely considered various pregnancies<sup>12</sup>. Normal explanations behind demonstrated preterm births incorporate pre-eclampsia or eclampsia. Disease is uncommon in late preterm deliveries however is available much of the time in which birth happens at under 30 weeks as appeared by histologic assessment of the foetal layers at delivery, concentrates from amniotic liquid from women in labour with unblemished layers and investigations of foetal layers from women with flawless films who experience caesarean area.

Preterm birth causes many minds overwhelming and the pathophysiology that triggers preterm birth is to a great extent known, anyway adding to the maternal foetal and placental inclining factors have been identified<sup>13</sup>. These incorporate ante partum haemorrhage, mechanical factors, for example, uterine over-extension and cervical ineptitude; hormonal changes and bacterial infection and aggravations<sup>15</sup>. Components that lead to preterm birth include social pressure, race, hereditary qualities, aggravation, and disease<sup>14</sup>. Infections by microorganisms have posed a potential threat as potential offenders of preterm birth. Chorioamnionitis identified by methods for clinical signs, histologic evidence and the way of life of microorganisms is the most evident case of infection related with early labour and delivery, Microbiologic proof recommends that disease may add to roughly 25% of preterm birth with bacterial colonization rates as high as 79% for birth at 23 weeks of incubation declining to 11% at 31 to 34 weeks Microorganisms included are organisms and microscopic organisms which will in general structure net labours or biofilms in which they are epitomized with a self-created polymeric lattice. In women in unconstrained preterm labour with flawless layers, the ordinarily recognized microscopic organisms are *Ureaplasmaurealyticum*, *Mycoplasma hominis*, *Gardenella vaginalis* and bacteriodes. Those frequently connected with chorioamnionitis and foetal disease after film crack are bunch B *Streptococci* and *Eschericia coli*<sup>6</sup>.

### **Microbial Infection of the maternal vagina and vulva**

There are three fundamental kinds of vagina and vulva diseases:

**Trichomoniasis** brought about by *Trichomonas vaginalis* which has related to a little danger of preterm delivery and low birth weight and the illness might be secure perinatally and happen in about 5% of infants destined to tainted mother<sup>14</sup>.

**Bacterial vaginosis (BV)** in pregnancy, there is significant proof that BV during is related with preterm delivery<sup>15</sup>. Other unfavourable results incorporate late unsuccessful labour, low birth weight, preterm premature rupture of membranes and postpartum endometritis<sup>16</sup>.

**Candidiasis**, which is caused by *Candida albicans*, candida colonization rates ascend from under 10% of pregnant women in the principal trimesters to over half in the third trimester<sup>17</sup>

### **Impact of microbiome during pregnancy**

The regularly acknowledged conviction that the child inside the uterus is sterile (while films are flawless) is being tested. It appears that maternal gut microbiota might have the option to translocate to the infant/placenta by means of the circulatory system. Also, the one-of-a-kind biological system of microbes in the placenta may start from the microorganisms of the mother mouth. Women' gut microbiota changes during pregnancy and this effects on digestion. So preferably, women need to head into pregnancy with a sound microbiome and afterward look after it. Tragically, our cutting-edge way of life isn't very microbiome agreeable, and huge numbers of us have dysbiosis (an awkwardness in gut microscopic organisms). Dysbiosis and a lot of 'inappropriate.

### **Factors Associated with Premature Delivery**

There is an immense contrast in pregnancy results between high pay and many centre and low salary nations. In some low-pay nations, the maternal mortality proportion is 100-overlap more noteworthy than in high-income countries (HIC). Regardless of whether both mother and baby endure, pregnancy difficulties or issues at delivery or during the neonatal period can prompt extreme maternal or newborn child morbidity<sup>18</sup>. As indicated by the world health organization (WHO) Nigeria had the most noteworthy, evaluated number of maternal deaths in Africa, and positioned eighth in the sub-Saharan district behind Angola, Chad, Liberia, Niger, Rwanda, Sierra Leone and Liberia<sup>10</sup>. Other Factors Associated with Premature are: Hardworking by

the mother, teenage pregnancy, use of inappropriate medications Sudden hypertension<sup>18</sup>

### **Colonisation of Human Microbiome**

The human body is a host for microbial populace which incorporate microorganisms, archaea, growths, and infections. Also, this contrast in microbiota synthesis at each body site are moulded by the fluctuating natural conditions, for example, pH, levels of oxygen, accessibility of supplements, dampness, and temperature as factor fundamental for development of microorganisms empowering different populaces to flourish and perform various capacities while associating with the human host<sup>19</sup>. These microbial networks majorly affect have wellbeing, by influencing host digestion<sup>20</sup>, insusceptibility<sup>21</sup> and hormones<sup>22</sup>. The larger part of organisms in the human body dwell in the gut, harbouring several bacterial species<sup>[23]</sup> of which the predominant bacterial phyla are Firmicutes and Bacteroidetes<sup>[24]</sup>. Moreover, the skin, vagina, and oral depression give significant specialties to bacterial networks, which add to the invulnerable framework by protection against potential pathogens<sup>21</sup>. A wide scope of variables can cause moves in the organization of the microbiota (named dysbiosis). Dysbiosis is normally connected with unsafe impacts and may have long haul results prompting infection. Instances of illness states related with dysbiosis incorporate corpulence, inflammatory bowel disease (IBD), diabetes, and metabolic disorder, on the other hand, there are common changes that happen in have related microbial creation all through host advancement—from earliest stages to youth, from youthful to senior grown-ups, and during pregnancy. While a portion of these progressions may appear to be indistinguishable from changes found in ailment states, in their exact formative setting, they don't prompt bleakness, yet rather advance wellness and endurance, and may along these lines be considered beneficial<sup>25</sup>.

### **Physiological Changes during Pregnancy**

After gestation or conceiving, the female body experiences hormonal, immunological, and metabolic changes to help foetal development and improvement<sup>26</sup>. During this period, levels of discharged hormones (particularly progesterone and oestrogens) rise significantly, and there are significant adjustments in the immune<sup>[26]</sup>. The immune changes are perplexing, and might be alluded to as safe adjustment, and level of safe concealment is expected to acknowledge the developing embryo bearing its own creating resistant framework, though then again, severe

insusceptibility must stay to shield the mother and baby from infections if this couldn't occur courses damage to the mother and the foetus. What's more, mitigating stages in mid-pregnancy, when the baby develops quickly<sup>27</sup>.

### **Factors Contributing to Prematurity**

There are number factors that add to the preterm delivery. This incorporates maternal age and wellbeing, event of past preterm birth, in-vitro preparation, low financial status (simultaneously there is an expansion in preterm birth in affluent networks), hereditary elements, rehashed third trimester premature birth, way of life and low birth weight<sup>26</sup>

### **Some Factors That Might Contribute to Preterm Birth Are:**

#### ***Cervical Cerclage***

Elective cerclage might be shown when there is an innate or procured shortcoming in the cervix that builds the danger recently unnatural birth cycle or preterm delivery.

#### ***Antibiotics***

Preterm delivery is regularly connected with proof of chorioamnionitis, and the previous the gestational age at delivery, the more prominent the hazard. Nonetheless, it is frequently not satisfactory whether infection or aggravation is the reason or an impact of preterm. This is additionally implying that woman consumed medications pointless may prompts impact of medications digestion which could course preterm delivery.

#### ***Steroids***

There is acceptable proof recommending that antenatal steroids ought to be given to moms who have compromised preterm work to lessen the frequency of neonatal respiratory pain disorder, this implies on the off chance that it isn't giving another preterm conveyed may happen as one of the contributory factors.

Natural factor in such a significant number of social orders a few women have the propensity for not visiting during pregnancy and this could course unexpected labour.

### ***Significance Role of Maternal Periodontitis in Preterm Birth***

Periodontal infection is one of the hazard factors related with preterm birth. Periodontal sickness is

a profoundly common irresistible and fiery ailment of tooth supporting tissues and if untreated can prompt oral disabilities<sup>28</sup> Periodontal ailment is brought about by principally Gram negative microaerophilic and anaerobic microscopic organisms that colonize the subgingival zone and produce noteworthy measures of ace incendiary mediators. Periodontal infection incorporates gum disease and periodontitis<sup>28</sup> Periodontitis is the nearness of gingival irritation at locales where there has been apical movement of the epithelial connection onto the root surfaces joined by loss of connective tissue and alveolar bone. Periodontitis go about as a far-off repository of the two organisms and provocative arbiters that may impact pregnancy and add to acceptance of preterm birth<sup>28</sup>. Periodontal microorganisms can go about as pathogens in the oral cavity as well as in other body regions because of the capacity of the microscopic organisms to quickly colonize, escape the host barrier component and produce substances that straightforwardly add to the annihilation of the tissues<sup>26</sup>. Periodontal pathogens or their result may arrive at the placenta and enter the amniotic liquid and foetal flow, serving to initiate fiery flagging pathways *Porphyromonas gingivalis* has been identified in the human placenta tissue of preterm yet not in term newborn children in that capacity *Porphyromonas gingivalis* is said to be related with preterm delivery<sup>28</sup>. Levels of *P. gingivalis*, *Fusobacterium nucleatum*, *Actinomyces actinomycetemcomitans*, *Tannerella forsythia* and *Capnocytophaga species* have been accounted for at fundamentally more significant levels in preterm deliveries when contrasted with term, periodontitis advances preterm birth for pregnant woman who are youthful, or HIV infected or have pre-eclampsia or pre-pregnancy obesity<sup>28</sup>.

### Management of preterm Birth

In the mid 1970s, a delayed course of antibiotic medication starting in the center trimester was found to decrease the recurrence of preterm delivery in woman who had asymptomatic bacteriuria and in the individuals who didn't, this treatment fell into neglect presumably because of antibiotic medication related tooth and bone dysplasias in the newborn children<sup>6</sup>.

As of late treatment for multi week or more with oral metronidazole and with erythromycin bring about a critical decrease in the occurrence of preterm delivery. Only with further information on the science of human parturition will advance be accomplished in forestalling rashness which is a

complex multifactorial issue. On the off chance that exploration is to majorly affect developing human weight of rashness skilled examinations from orders should cooperate sharing databases biologic examples and scholarly points of view<sup>13</sup>.

### Application of antenatal corticosteroids in the treatment of preterm birth

Preterm birth is presently considered as the most widely recognized reason for neonatal mortality around the world, to lessen neonatal mortality worldwide and dreariness related with preterm birth, antenatal corticosteroids are ordinarily utilized in woman in danger to convey preterm in both high salary nations and center pay countries.<sup>29</sup> Overall when antenatal corticosteroids are given to the mother in those settings somewhere in the range of 24 and 34 weeks of incubation at 12-24 hours before delivery and delivery happens inside 7 days, there is 31% decrease in neonatal mortality because of diminished danger of respiratory locale disorder, intraventricular discharge, necrotizing enterocolitis and other pleotropic impacts that improve newborn child outcomes<sup>26</sup>To address the absence of data on the effect of antenatal corticosteroids in low and centre pay nations. The antenatal corticosteroids in Zambia, Kenya, Pakistan and India demonstrated an expansion in the diminish danger of preterm from 10% to 46% in the control bunches<sup>31</sup>.

### CONCLUSION

The microbiota can course damage to woman and prompting unexpected labour in preterm moms. It can likewise fill in as recipient ordinary greenery to woman vaginal by repressing the development of undesirable microorganisms. Preterm births supposedly were higher in the lower class than the centre and upper social class this is because of obliviousness, lack of healthy sustenance and poor maternal wellbeing. Some microbes can likewise be taken as probiotics medication or supplement to give sustenance to human particularly preterm moms

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## Reference

- Bezerra LC, Oliveira SMJV, Latorre MRDO. Prevalência e fatores associados à prematuridade entre gestantes submetidas à inibição de trabalho de parto prematuro. *Rev Bras Saúde Mater Infant* 2006;6:223-9.
- Rades E, Bittar RE, Zugaib M. Determinantes diretos do parto prematuro eletivo e os resultados neonatais. *RBGO* 2004;26:655-62.
- Bittar RE, Carvalho MHB, Zugaib M. Condutas para o trabalho de parto prematuro. *RBGO* 2005;27:561-6.
- Gonçalves Carla Vitola, Duarte Geraldo, Costa Juvenal Soares Dias da, Marcolin Alessandra Cristina, Bianchi Mônia Steigleder, Dias Daison *et al.* Diagnosis and treatment of cervical cancer during pregnancy. *Sao Paulo Med J* 2009;127:359-65.
- Spindola T, Silva LFF. Epidemiological profile of teenagers met in a prenatal teaching hospital. *Anna Nery Rev Enferm* 2009;13:99-107.
- Robert LG, John CH, William WA. No Title intrauterine infection and preterm delivery. *N Engl J Med* 2000;342:1500-7.
- Cappelletti M, Presicce P, Lawson MJ, Chaturvedi V, Stankiewicz TE, Vanoni S. *et al.* Type I interferons regulate susceptibility to inflammation-induced preterm birth. *JCI insight* 2017;2
- Abdulkadir B, Aisha AS, Ummasalmah AS, Mujahid NS, Musa SK, Yusuf A. *et al.* The Effect of Microbial infections in Maternal Premature Delivery: An African Context. 2016;5:2
- Dey AC, Mannan A, Saha L, Hossain I. Review Article Magnitude of Problems of Prematurity- National and Global Perspective : A Review 2012;36:146–52.
- Jammeh A, Sundby J, Vangen S. Maternal and obstetric risk factors for low birth weight and preterm birth in rural Gambia: a hospital-based study of 1579 deliveries, 2011;94–103.
- Abiodun O, Francis B. Factors Associated with Spontaneous Preterm Delivery in a Nigerian Teaching Hospital 2014;29: 9–14.
- Robert LG. John CH. William WA. No title intrauterine infection and preterm delivery. *N Engl J Med* 2008;342:1500-7
- Louis JM. M.D. Ph.D. Michael KM D. The Enigma Of Spontaneous Preterm Birth. *N Engl J Med*, 2010;362:529-35.
- Sherrard J. National guideline on the management of *Trichomonas vaginalis*. *Eur Guiman vag disc* 2001;12:73-77
- Hillier SL, Nugent RP, Eschenbach DA. Association between bacterial vaginosis and preterm delivery of a low birth-weight infant. *N Eng j med* 1995;333:1737-42.
- Hay P. National guideline for the management of bacterial vaginosis. *BMJ* 2007;335:1147
- Wang E, Smaill F. Infection in pregnancy. In: Chalmers I, Enkin M, Keirse M editors. *Effective care in pregnancy and childbirth*. Oxford: Oxford University press; 1989. p.534-64.
- Young GL, Jewell D. Topical treatment for vaginal candidiasis (thrush) in pregnancy (Cochrane Review). In: *The Cochrane Library* Oxford, 2003;3:
- Kassebaum NJ, Bertozzi-villa A, Coggeshall MS E. Global, regional, national levels and causes of maternal mortality during 1990-2013: A systematic analysis of the global burden of disease study. *Lancet* 2014;384: 980-1004.
- Ursell LK, Clemente JC, Rideout JR, Gevers D, Caporaso JG, Knight R. The interpersonal and intrapersonal diversity of human-associated microbiota in key body sites. *J. Allergy Clin. Immunol* 2012;129:1204–8.
- Turnbaugh PJ, Ley RE, Mahowald MA, Magrini V, Mardis ER, Gordon JI. An obesity-associated gut microbiome with increased capacity for energy harvest. *Nature* 2006;444:1027–31.
- Naik S, Bouladoux N, Wilhelm C, Molloy MJ, Salcedo R, Kastenmuller W, *et al.* Compartmentalized control of skin immunity by resident commensals. *Science* 2012;337: 1115–19.
- Neuman H, Debelius JW, Knight R, Koren O. Microbial endocrinology: the interplay between the microbiota and the endocrine system. *FEMS Microbiol. Rev* 2015;39:509–21.
- Prof Robert LG, Jennifer FC PhD, P. R. M. No Title. *Epidemiology and Causes of Preterm Birth* 2008;371:75–84.
- Lozupone CA, Stombaugh JI, Gordon JI, Jansson JK, Knight R. Diversity, stability and resilience of the human gut microbiota. *Nature* 2012;489,220–30.
- Rajilic-Stojanovic M, Heilig HG, Molenaar D, Kajander K, Surakka A, Smidt H. *et al.* Development and application of the human intestinal tract chip, a phylogenetic microarray: analysis of universally conserved phylotypes in the abundant microbiota of young and elderly adults *Environ Microbiol* 2009;11:1736–51.
- Spor A, Koren O, Ley R. Unravelling the effects of the environment and host genotype on the gut microbiome. *Nat Rev Microbiol* 2011;9:279–90.
- Kumar P, Magon N. Hormones in pregnancy. *Niger Med J*. 2012;53:179–83.
- Mor G, Cardenas I. The immune system in pregnancy: a unique complexity. *Am J Reprod Immunol* 2010;63:425–33.
- Du, Minquan Ren, Hongyu. Role of Maternal Periodontitis in Preterm Birth. *Frontiers in Immunology* 2017;8:10-3389
- Elizabeth M, Mc Clure, Robert LG, Alan HJ, MM. Reducing neonatal mortality associated with preterm birth. *inter j obs gyn* 2016;13:61