

Achieving Complete Immunization Status per Age to Reducing Risk of Acute Respiratory Infections (ARIs) among Infants in Nigeria: What should be done?

Ibama, A.S.^{1*}, Amadi, A.N.², Ibulubo, R.I.³, Timothy, T.⁴ and Risikat, M.O.⁵

¹University of Port Harcourt, Port Harcourt, Nigeria.

²Federal University of Technology, Owerri, Nigeria.

³Rivers State College of Health Science & Management Technology, Port Harcourt, Nigeria.

⁴Ignatius Ajuru University of Education, Port Harcourt, Nigeria.

⁵University College Hospital, Ibadan, Nigeria.

*Correspondence:

Ibama, A.S., University of Port Harcourt, Port Harcourt, Nigeria.

Received: 25 Apr 2022; Accepted: 26 May 2022; Published: 30 May 2022

Citation: Ibama, AS, Amadi, AN, Ibulubo, RI. Achieving Complete Immunization Status per Age to Reducing Risk of Acute Respiratory Infections (ARIs) among Infants in Nigeria: What should be done?. Int J Family Med Healthcare. 2022; 1(1): 1-7.

ABSTRACT

Immunization status as an outcome measure of vaccination is very critical in the prevention and control of vaccine preventable diseases. Irrespective of several improvements in child survival strategies for over 3 decades, ARI still ranks among diseases such as malaria, diarrhea and measles responsible for majority of deaths among infants and young children in Nigeria and other developing countries. Immunity is a mechanism and process of the body system for preventing diseases by way of innate and adaptive/acquired means. This review paper, aimed at taking a critical look at how pattern of uptake of vaccination among infants according to the National Immunization Schedules under the classification of partial, complete and non-immunization status influence risk of ARI among infants. In view of this, a review of the essential literature was conducted to establish relevant concepts and evidences. It has been revealed from survey that, only 21% children had received all age-appropriate vaccinations and that 19% of children in Nigeria have not received any vaccinations. In addition, among several other studies, it was equally revealed that the Risk of ARI was higher among infants with none immunization (none and some uptake of vaccines per age) status with statistical significance ($OR=1.97 \approx 2$, ($p<0.0001$, $95\%CI=1.495-2.604$). Meaning infants with none immunization status per age are about 2 times at Risk of contracting ARI compared to infants with complete immunization status per age in Nigeria. Hence, from the principles and mechanisms of immunization responses and evidence-based reports, it is very clear that complete immunization status per age among infants is capable of reducing the Risk of ARI in that age group. Therefore, what should be done as enumerated in this publication need to be given required attention to achieving reduction in the burden of ARI among infants in Nigeria.

Keywords

Complete immunization status, Partial immunization status, Immunity, National Immunization Schedule, Acute Respiratory Infection, Risk factor, Vaccination.

Introduction

Vaccination as a concept is a method and practice concerning the activation and or maintenance of the body immune system over time, via the introduction of antigens (vaccines) into the body system. Immunity is the key entity in disease prevention,

which vaccination as a health care delivery strategy and practice is designed to achieve. Methods of acquiring immunity basically include; Innate (Natural Immunity) – via maternal antibodies transfer, which goes away during the first year of life and acquired/ adaptive immunity (via antibody and cell-mediated constituents) – immunity gotten through either suffering from the disease or through vaccination of specific antigens involving production of antibodies by the immune system [1]. The basic tool for actualization of immune state is vaccines, which were developed and or prepared in such a manner to containing the same antigens

(or parts of antigens) that cause diseases. But the antigens in vaccines were either killed or weakened to the point that they do not cause ailment. Nevertheless, they are strong enough to make the immune system produce antibodies that lead to immunity devoid of suffering from the disease it prevents, which overtime leads to definable immunization status.

Partial immunization status per age is the uptake of some vaccines per age according to National Immunization Schedules and it is a critical matter in the effective prevention and control of vaccine preventative diseases, while complete immunization status per age is the uptake of all vaccines per age according to National Immunization Schedules. Whereas non-immunization status per age is the non-uptake of vaccines per age according to National Immunization Schedules.

It was stated that in the overall, 31% of children have received all basic vaccinations and 21% have received all age-appropriate vaccinations and that 19% of children in Nigeria have not received any vaccinations [2]. However, these data reflect some improvements within the last five years as assessed, but the question is, will such situation enable us achieve the elimination of vaccine-preventable diseases and translate to achieving the reduction of ARI in our context? Risk factors are factors linked to the host and or environment that increase the chances of morbidity and or severity of ARI in less than one-year children, in the present context, focusing on immunization status. ARIs include a wide range of upper and lower respiratory tract infections (pneumonia etc.), commonly manifesting with cough, fever, and rapid breathing [3]. More so, ARIs are heterogeneous and complex group of ailments caused by a wide range of pathogens, including human coronavirus in which the possible anatomic site/s extends from the pharynx to the alveoli [4,5]. Its onset is sudden in any part of the respiratory system from noses to alveoli, including para-nasal sinuses and middle ear and pleural cavity (See figures 1, 2 and 3).

Burden of ARI

Studies and publications revealed that ARI is a major public health problem in both developed and developing countries. However, it

poses as a leading cause of ailment and death in many developing countries including Nigeria. It is known that host factors such as immunization status is implicated in the susceptibility potential to ARI among infants. In midst of several improvements in child survival strategies for over 30 years, ARI still ranks among diseases such as malaria, diarrhea and measles responsible for majority of deaths among infants and young children in Nigeria and other developing countries.

In 1998, estimates of annual mortality rate of ARI in infants range from 1.5/1,000 in North America to from 11 to 15 per 1,000 in Central and South America and Africa. In 1999, annual morbidity and mortality from ARI for infants in Nigeria was estimated at 15% and 22% respectively. It was also indicated that 2% of children under 5years were ill with cough and rapid breathing, symptoms of ARI, in the 2weeks before the survey [6]. The prevalence at age <6months and 6-11months were 1.5% (2,989) and 2.9% (3,263) respectively, meaning a total prevalence of 4.4% (290,400 cases) among infants (See figure 4 for Schematic illustration). However, the report was not disaggregated to show the extend of burden of ARI among Infants [2].

National Routine Immunization Schedule for Infants

Table 1: Vaccine Uptake Schedule as per Age according to National Immunization Programme.

Age	Vaccine
Birth	Bacillus Calmette Guerin (BCG); Oral Polio Vaccine-0(OPV-0), Hepatitis B Vaccine (HepB-0)
6 weeks	OPV-1; Pentavalent-1; Pneumococcal Conjugate Vaccine (PCV-1); IPV1
10 weeks	OPV-2; Pentavalent-2; PCV-2
14 weeks	OPV-3; Pentavalent-3; PCV-3, IPV2
9 months	Measles 1; Yellow Fever, Conjugate Meningitis A (Men. A) Vaccines
Note: OPV-0 and HepB-0 must be given before the age of 2weeks.	

Mechanism of Primary Vaccination Response

It had been reported that when vaccination is given such as shown in Table 1 and antigens (microorganisms) are encountered for the first time there is a *primary response* in which a low level of

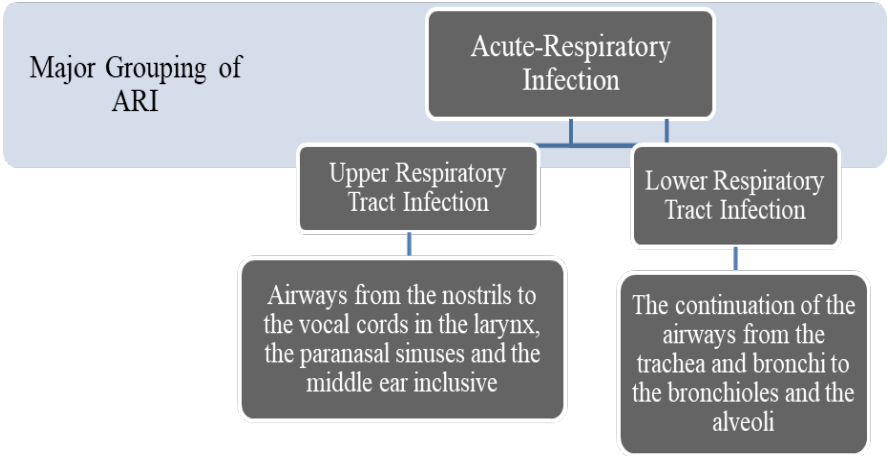


Figure 1: Major grouping of ARI.

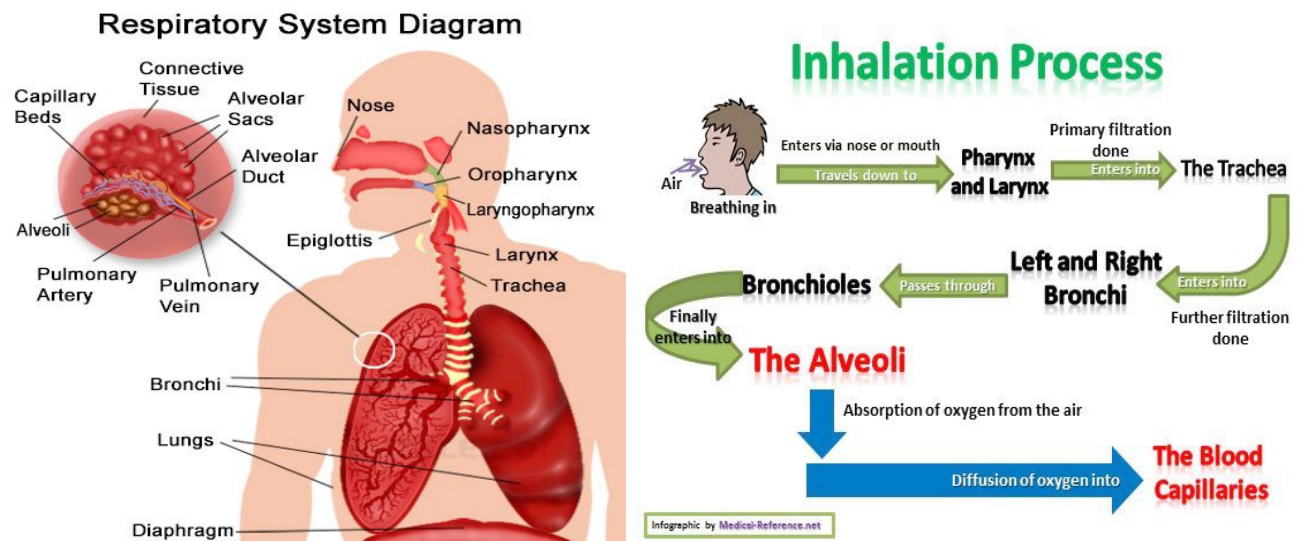


Figure 2: Respiratory System and Inhalation Process.

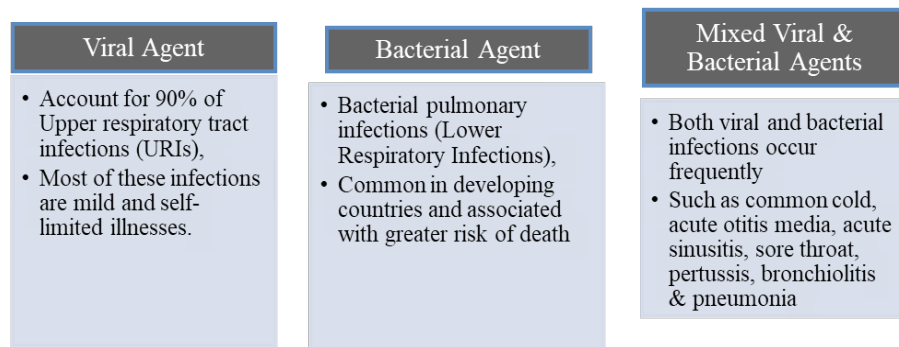


Figure 3: Causes of ARI.

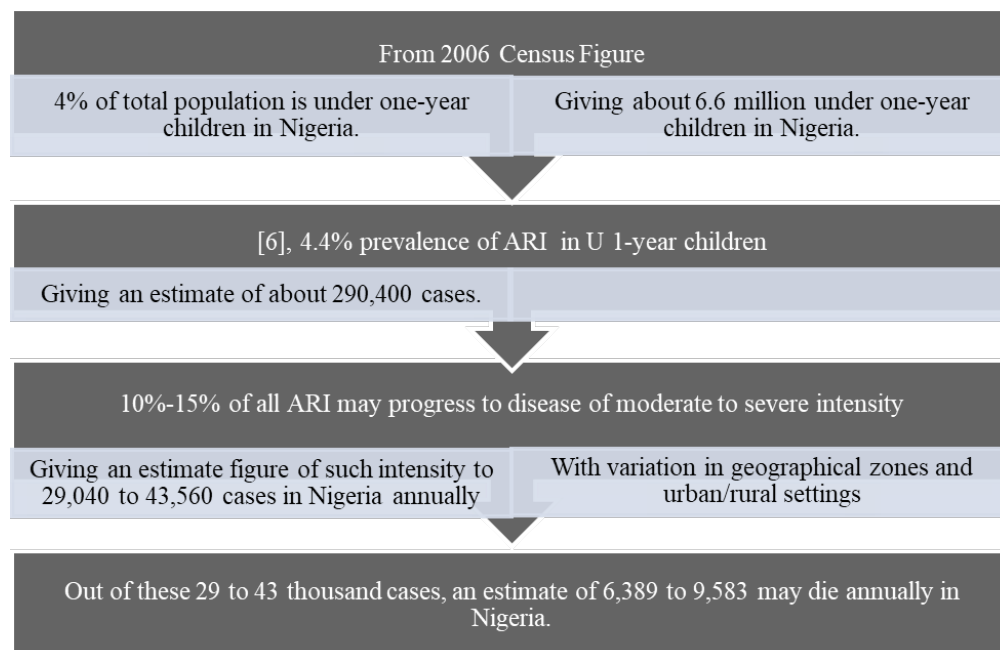


Figure 4: Burden of ARI among Infants in Nigeria.

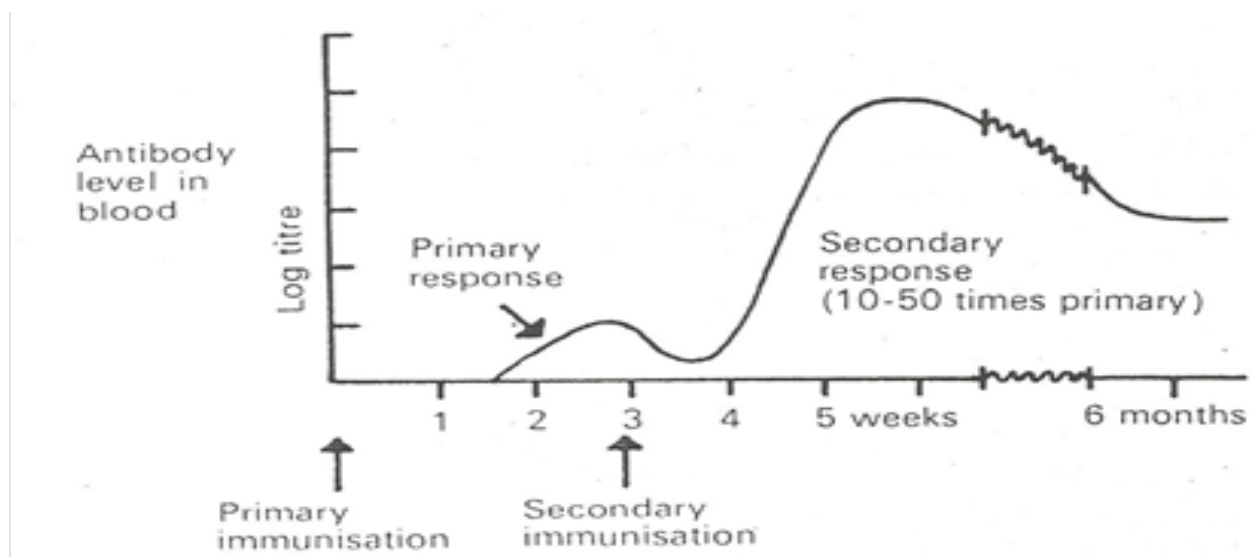


Figure 5: The Antibody Response to Immunization. (Source: [7])

antibodies can be detected in the blood after about two (2) weeks. Although the response may be sufficient to overcome the antigen, the antibody levels then fall unless there is another encounter with the same antigen (vaccination) within a short period of time (say 4 weeks) for multiple doses vaccines. In the case of COVID-19, vaccine is still under study for effectiveness and efficiency among this group of persons.

Mechanism of Secondary Vaccination Response

Subsequent vaccination of specific antigens produces a *secondary response* in which there is rapid response by memory B-cells resulting in a marked increase in antibody production. Further increase can be recorded by later encounters (vaccinations), such as supplemental immunizations/vaccinations or according to immunization schedules per age, but eventually a maximum is reached. This is the principle behind active immunization programme against infectious diseases [1,7].

This implies that partial uptake of vaccines per age lacks systemic mechanisms capable of producing sustainable *secondary responses* in increasing antibody production within definable period in fighting specific pathogens, rather even the *primary response* antibody level will keep depleting as pathogens are encountered, thereby making such partial uptake of vaccines to be as good as none uptake of vaccine in disease prevention and control principle [8]. (See figure 5 for graphical illustration).

Link between Vaccines and Autoimmune Diseases?

Diseases attributable to autoimmune condition occur when the body reacts against itself. Such diseases include; Guillain-Barre Syndrome (GBS), multiple sclerosis, and diabetes. Autoimmune condition can be triggered by genetic predispositions. However, it can also be induced by bacterial or viral infections, for instance, campylobacter – an intestinal bacterial infection can cause GBS (a disease of the peripheral nervous system). In addition, Influenza virus can exacerbate symptoms of multiple sclerosis (a disease of

the central nervous system). Equally, Coxsackie virus can cause diabetes by inducing reaction of the body against cells in the pancreas that make insulin [9].

The controversy in linking vaccines to autoimmune conditions was drawn from the basis that natural infections can lead to autoimmune conditions without reasonable evidence-based reports. So, we shall briefly explore to what extent the link between vaccines and autoimmune diseases is justified, noting its capability in the promotion of vaccine hesitancy thereby hindering the achievement of complete immunization status among infants' overtime. Reports have revealed that there has not been any consistent link between vaccines and autoimmune conditions. In some studies influenza vaccine was shown to have attributable risk of 1GBS/1,000,000 vaccine recipients, comparing this with the natural influenza infection attributable to 17GBS/1,000,000 infected persons, we could conveniently adduce that influenza vaccine prevent more common cause of GBS [9].

Nevertheless, Centre for Disease Control and Prevention; suggest a precaution for influenza vaccination, if anyone develops GBS within 6weeks of receipts of an influenza vaccine. In addition, for tetanus-containing vaccines – anyone that developed GBS within 6weeks of receipt of a tetanus-containing vaccine should have a precaution related to future receipt of such vaccines, but if their bout of GBS is outside the range of 6weeks, they can continue with the vaccination. In all of these, it is worthy of note that, MMR (measles, mumps, rubella), Human papilloma virus (HPV), meningococcal conjugate, polio, pneumococcal, varicella (chickenpox), haemophilus influenza type b (Hib), rabies, hepatitis A, and B vaccines are not associated with an increased risk of GBS.

Therefore, holding on to the notion, vaccines do not cause autoimmune conditions, is justified, noting that vaccines do not drive immune response nearly as vigorously as natural infections do, until otherwise proven by evidenced-based reports.

The Respiratory Tract and Immune Response

In the absence of an organized and systemic immune response, antibiotics alone were usually incapable of eradicating bacterial pathogens [10]. This was in line with earlier opinion that antibiotics only had slight effect on early death from bacteremia and sepsis due to *Streptococcus pneumoniae* [11]. The innate immune response provides a first line of defense against infection (See Table 2). In this regard, it had been estimated that the innate immune system provides protection against 98% of encountered pathogens [12].

The upper respiratory tract is the ecological niche for many bacterial species among which were the normal flora (commensals) such as, *Streptococcus pneumoniae* together with *Haemophilus influenzae*, *Staphylococcus aureus*, *Moraxella catarrhalis*, and various haemolytic streptococci, *S. pneumoniae* colonizes the nasopharyngeal tract [13].

It was stated that effectual respiratory tract host defense against pathogens depends on the interaction of type-specific antibodies, complement, and neutrophils or other phagocytic cells [14,15]. If pathogens overpower these defenses and gain entry into the blood stream, ant capsular antibodies mediate systemic protection [16].

A reduced mucosal immune response might lead to persistent and recurrent colonization and subsequent infection, whereas an efficient local immune response to the pathogen eliminates colonization and prevents re-colonization [17]. In a general analysis, [17] stated as thus, “the mucosal immune system develops faster than the systemic immune system, and functions from the age of 6 months” while [18], has this to say, “IgG and secretory IgA antibodies directed against capsular polysaccharides and surface-associated proteins had been observed in saliva of children under five years in response to colonization with *S. pneumonia*”.

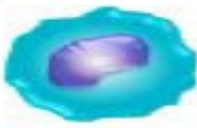
COMPONENTS	FUNCTION
Macrophage 	• Phagocytosis • Activation of bactericidal activity • Antigen presentation
Dendritic cell 	• Antigen uptake in the periphery • Antigen presentation
Neutrophil 	• Phagocytosis • Activation of bactericidal activity
Other myeloid cells (eg, eosinophils, basophils, mast cells) 	• Kill antibody-coated parasites • Release histamine granules and other pro-inflammatory mediators
Natural Killer cells 	• Release lytic granules to kill some virus-infected cells
Complement 	• Soluble proteins that form a complex to destroy microorganisms
Cytokines 	• Proteins secreted by cells that affect the behavior of nearby cells bearing appropriate receptors

Table 2: Components of Innate and Adaptive (Acquired) Immunity.

The innate components, including macrophages; neutrophils; myeloid cells; natural killer cells are essential for the control of common bacterial infections, but cannot always eliminate infectious organisms, as they cannot recognize some pathogens because of specific protective capsules. In addition, viruses are rarely recognized.

The adaptive components via dendritic cells by way of secretion of cytokines and complements to activate lymphocytes of adaptive immune response to overcome the shortcomings of innate immune response, so, recognition of infinite different antigens, and being targeted specifically.

Evidence-Based Relationship between Immunization Status and Risk of ARIs among Infants

A study from West Tripura noted that the incidence of respiratory infection was higher among non-immunized children [19]. Inappropriate immunization for age was significantly related with ARI in U5yrs children in Delhi study [20]. A hospital-based prospective study conducted in Kolkata found that non-immunization was a significant risk factor for ARI [21]. The study by [22], revealed that immunization appears to be strongly associated with severity of ARI cases. This result was consistent with results found by in Iraq and in India [20,23]. A cross sectional study covering 500 under five years' children in urban and rural areas of Ahmedabad district, showed direct correlation between immunization status of children and occurrence of ARI. It was least in children who were fully immunized (9.1%) as compared to unimmunized children (33.7%). This disparity was statistically significant ($x = 33.87$, $p < 0.001$), [24].

A community-based cross-sectional study in 21 registered urban slums of Guwahati in Assam, India among 370 U5yrs children, showed that non-immunized children had more chances of developing ARI (RR = 2.01). Complete immunization among ARI cases was only 10%. In the non-immunized group ARI cases was noted as 57.5%. In this study, children with completed primary immunization status were combined with those partially immunized and were compared with non-immunized children in determining the risk for ARI in relation to immunization status, [25].

In the study by [26], involving 436 U5yrs children diagnosed with ARI in three hospitals in Enugu, Nigeria, poor immunization status was found to significantly affect the prevalence of ARI, 50% of poorly immunized subjects had severe forms of ARI. This is consistent with previous reports [24,27].

The study of 1,100 infants in Rivers State, Nigeria by [8], revealed that the occurrence of ARI was higher among infant cases with none immunization (none and some uptake of vaccines per age) status (56.4%), than their control subjects (39.4%) with a statistical difference of 17.0% frequency of occurrence. In this study the Risk of ARI was higher among infants with none immunization (none and some uptake of vaccines per age) status with statistical significance (OR=1.97 $\approx$ 2, ($p < 0.0001$, 95%CI=1.495-2.604).

Meaning infants with none immunization status per age are about 2 times at Risk of contracting ARI compared to infants with complete immunization status per Age in Nigeria.

Conclusion

It is obvious from the principles and mechanisms of immunization responses and evidence-based reports that complete immunization status per age among infants is capable of reducing the Risk of ARI in that age bracket. Therefore, the should be done as enumerated in this publication need to be given required attention to achieving reduction in the burden of ARIs among infants in Nigeria.

What should be done to Reducing Immunization Status Influenced Risk of ARIs among Infants in Nigeria? (Recommendation)

1. Routine immunization activities should be strengthened with aggressive and consistent outreach/home-based services.
2. Intensive tracking and detection of defaulting vaccination/immunization uptake per age according to National Immunization Programme Schedules among infants by all Stakeholders.
3. All Stakeholders and Partners should regularly and timely make adequate logistic provision and necessary stipends available for all routine immunization activities.
4. Accountability of all Immunization activities should be given priority attention.

References

1. Centers for Disease Control and Prevention (CDC), (2014), Why are Childhood Vaccines so Important? National Centre for Immunization and respiratory Diseases, May 19, 2014.
2. Nigeria Demographic and Health Survey (NDHS) report. 2018.
3. Health Reform Foundation. Nigerian Health Review. Ibadan, Nigeria. Kenbim Press Limited. 2006.
4. Johnson, A-W BR, (2007). Acute respiratory infections. In: Azubuike, J.C., Nkanginieme, K.E., editors. Paediatrics and Child Health in Tropical Region. 2nd ed. Owerri African Educational Services; 2007. pp. 396–425.
5. Moore H. Acute lower respiratory infections (ALRI) in Indigenous and non-Indigenous children. Australasian Epidemiologist. 2011; 18: 15-20.
6. Nigeria Demographic and Health Survey (NDHS) report. 2013.
7. Ibama, A. S. (2011). Step-By-Step Approach to Clinical Procedures in Primary Health Care. 1st ed. Etuk Concepts, Port Harcourt, Nigeria.
8. Ibama AS, Dozie INS, Abanobi OC, et al. Immunization Status in the Pattern and Risk of Acute Respiratory Infection among Infants in Rivers State, Nigeria. Acta Scientific Paediatrics. 2019; 70-79.
9. <https://www.chop.edu/centers-programs/vaccine-education-center/vaccines-and-other-conditions/vaccines-and-autoimmune-diseases>.

10. Ambrus JL, Ambrus JL. Nutrition and infectious diseases in developing countries and problems of acquired immunodeficiency syndrome. *Exp Biol Med*. 2004; 229: 464-472.
11. Hedlund J. Community-acquired pneumonia requiring hospitalization. Factors of importance for the short-and long-term prognosis. *Scand Journal of Infectious Disease*. 1995; 97: 1-60.
12. Jones GE. Cellular signaling in macrophage migration and chemotaxis. *J Leukoc Biol*. 2000; 68: 593-602.
13. Paton JC, Andrew PW, Boulnois GJ, et al. Molecular analysis of the pathogenicity of *Streptococcus pneumoniae*: The role of pneumococcal proteins. *Annual Review of Microbiology*. 1993; 47: 89-115.
14. Gordon SB, Irving GR, Lawson RA, et al. Intracellular trafficking and killing of *Streptococcus pneumoniae* by human alveolar macrophages are influenced by opsonins. *Infectious Immunology*. 2000; 68: 2286-2293.
15. Gingles NA, Alexander JE, Kadioglu A, et al. Role of genetic resistance in invasive pneumococcal infection: Identification and study of susceptibility and resistance in inbred mouse strains. *Infectious Immunology*. 2001; 69: 426-434.
16. Anttila M, Voutilainen M, Jantti V, et al. Contribution of serotype-specific IgG concentration, IgG subclasses and relative antibody avidity to opsonophagocytic activity against *Streptococcus pneumoniae*. *Clin Exp Immunol*. 1999; 118: 402-407.
17. Rodríguez L, Cervantes E, Ortiz R. Malnutrition and Gastrointestinal and Respiratory Infections in Children: A Public Health Problem. *International Journal of Environ Res Public Health*. 2011; 8: 1174-1205.
18. Bogaert D, de Groot R, Hermans PWM. *Streptococcus pneumoniae* colonisation: The key to pneumococcal disease. *Lancet Infectious Disease*. 2004; 4: 144-154.
19. Deb SK. Acute respiratory disease survey in Tripura in case of children below five years of age. *Journal of Indian Medical Association*. 1998; 96: 111-116.
20. Broor S, Pandey RM, Ghosh M, et al. Risk Factors for Severe Acute Lower Respiratory Tract Infection in Under-Five Children. *Indian Pediatrics*. 2001; 38: 1361-1369. <http://www.indianpediatrics.net/dec2001/dec-1361-1369.htm>
21. Das Pk, Saha JB, Basu K, et al. Some clinic-epidemiological aspect of bronchiolitis among infants and young children-A hospital-based study. *Indian Journal of Public Health*. 2003; 47: 66-71.
22. Thamer K, BAN A. Epidemiology of Acute Respiratory Tract Infections (ARI) Among Children Under Five Years Old Attending Tikrit General Teaching Hospital. *Middle East Journal of Family Medicine*. 2006. <http://www.mejfm.com/journal/May2006/epidemiology.htm>
23. Al-Humairy EH. Risk factors of severe pneumonia in children. A thesis submitted to the Iraqi committee for medical specialization in partial fulfillment of the requirement for the degree of fellowship of Iraqi committee for medical specialization- pediatrics. *The Iraqi Journal of medical sciences*. 1998; 4: 20-25.
24. Prajapati B, Talsania N, Lala MK, et al. A study of risk factors of acute respiratory tract infection (ARI) of under-five age group in urban and rural communities of Ahmedabad district, Gujarat. *health line*. 2012; 3: 1-5.
25. Islam F, Sarma R, Debroy A, et al. Profiling Acute Respiratory Tract Infections in Children from Assam, India. *Journal of Global Infectious Disease*. 2013; 5: 8-14.
26. Ujunwa FA, Ezeonu CT. Risk factors for Acute Respiratory Tract Infections in Under-Five Children in Enugu Southeast Nigeria. *American Medical Health Sciences Research*. 2014; 4: 95-99.
27. Oyejide CD. Review of epidemiological risk factors affecting the pathogenesis of acute respiratory infections. *Nigerian Journal of Paediatrics*. 1988; 15: 1-9.