



Contents of Research Activities in Immunology Unit of a Tertiary Institution in Ibadan, Southwestern Nigeria

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Author's contribution

This whole work was carried out by the author OGA.

Review Article

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ABSTRACT

Background: Immunology laboratories carry out researches and training coupled with accurate diagnosis and prognosis of diseases for effective treatment and elimination of diseases. Information on the patterns of research activities in Immunology laboratories in developing countries is scarce.

Aims: This review of pattern of research activities in Immunology Unit of Department of Chemical Pathology, University Of Ibadan, Nigeria aims to provide useful information on outcomes of researches carried out by eminent Nigerian Immunologists so as to provide template for designing further immunological studies. This review also provides basis for more intensive immunological studies on Nigerians exposed to environmental or occupation chemicals which is yet to be extensively explored. The applications of the research outcomes on diagnosis and management of patients is also stressed.

Design: A retrospective review of research activities in Immunology Unit of the Department of Chemical Pathology, University of Ibadan, Nigeria till May 2012 was done. Major contributions to knowledge and diagnostic importance of results were enumerated.

Results: Majority of the specimens processed for researches were blood, breast-milk, saliva and urine. The subjects recruited were those with malaria parasitemia, urinary schistosomiasis, malnutrition, cancers, HIV infection, pulmonary tuberculosis, periodontitis, pregnancy, neonates, different age groups, different social life-styles and those exposed to chemicals. Most of the immunological studies were carried out on subjects with infectious agents or parasites but little emphasis was placed on

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immunological studies during physiological diseases, social life styles or exposure to environmental agents.

Keywords: Immunology; infections; occupational exposure; future; Nigeria.

1. INTRODUCTION

Immunology is an inter-disciplinary science and immunological techniques are required for a wide variety of investigative work in diagnosis and research. The Science of immunology is dynamic in nature and a full understanding of its basic principles is very vital. Immunology has played significant roles in effective treatment of diseases through development of antibody. It is the knowledge of immunology that paves way to the elimination of small pox and the effective control of poliomyelitis world-wide [1]. Furthermore, most of the problems associated with replacement and transplant surgery have been overcome through the proper understanding of the science of immunology [2]. It is therefore clear that immunology cuts across all disciplines in biological, medical or veterinary sciences. In University of Ibadan, Nigeria, immunology has been carefully structured and firmly rooted in Department of Chemical Pathology for above forty years.

In 1965, immunology training commenced to attendees from African Countries and beyond in the WHO Immunology Research and Training Centre, sited in the Department of Chemical Pathology of University of Ibadan, Nigeria.

The main aim of establishing this Immunology Research and Training Unit was

- (1) To conduct outstanding researches in immunology using available resources and to provide up-to-date information on modern concepts and practice of Immunology, with the hope that knowledge gained would be usefully applied in laboratories, clinics, or classrooms. Researches in Immunology Unit have been extensive as demonstrated by the works supervised or carried out by previous Heads and Professors of Unit (Profs Houba V, Osunkoya B.O, Williams I.A, Salimonu L.S) and Prof O.G. Arinola.
- (2) Also, the Unit was established to give basic training to individuals who may eventually choose Immunology as a career, as well as to individuals who are already specialists in some field(s) of bio-medicine, and who may find a knowledge of Immunology useful in their fields of specialty. Immunology Training Program provides academia, industry, and governmental research laboratories with highly creative and productive research immunologists.
- (3) Most immunological diseases are life-long and can be expensive to manage. Early and accurate detection is very important. The Unit provides an introduction to the basics of immuno-pathology and clinical immunological investigations, so as to analyse (diagnosis) and solve immunological problems. Two basic types of laboratory tests were common in the Unit: Serology and Leucocyte analysis in which components of blood, seminal fluid, saliva and urine were analysed to detect/measure one or all of these: antibodies, leucocyte migration, leucocyte engulfing, leucocyte intracellular killing, complement factors, cytokines, immune complexes and immunoglobulin levels. Lately additional tasks include hypersensitivity testing and Skin prick test to monitor and diagnose allergies. All

these tests may be diagnostic, or may measure the pathology of a disease or may provide insight for prognosis.

2. MAJOR CONTRIBUTIONS OF RESEARCHES CONDUCTED IN IMMUNOLOGY UNIT OF UNIVERSITY OF IBADAN, NIGERIA (Till 2012)

The major contribution to knowledge and development of science in immunology are summarized below.

2.1 Immunology of Nigerians with Plasmodium Malaria Parasites

The following conclusions were drawn on immunological studies of Nigerians infected with the malaria parasite across all age groups:

Transfer of maternal antibodies to the foetus was found to involve principally IgG antibodies. However, foetuses were capable of synthesizing IgG antibodies in response to antigenic stimulation. After birth, the initial response of African infants to malaria was the production of IgM but in the adult, malaria infection resulted in increased production of IgG and particularly IgM. This study also confirmed the transplacental transfer of *P. falciparum*-specific antibodies and the higher incidence of malaria parasitaemia in primiparae. The presence of *P. falciparum*-specific IgM in some cord samples was suggestive of intrauterine sensitization of the foetus to malarial antigens [3]. Moreover, inter-pregnancy interval affected acquired malaria specific immunity [4].

The rapid decrease in the density of the malaria parasite after 2months of age and the rapid decline in antibody levels to about half the birth level at 2months of age as reported by Achidi et al. [5] suggested that protection of the African infant against clinical malaria is limited to the first two months of life [5].

Most Nigerian infants were found to experience their first episode of clinical malaria between 3 and 6 months of age (early in life). Haemoglobin genotype, PCV of cord blood, birth weight and MNSsU blood group did not significantly alter the onset of clinical malaria in these infants. The finding of an active antibody response to malarial antigens in infancy (after 4 months of age) encouraged the hope that a malaria vaccine administered early in life may accelerate the development of naturally acquired immunity and thus protect the population most at risk [3,6].

Nigerian adults including pregnant women were found to be carriers of low grade asymptomatic malaria suggesting that immunity against malaria is not sterile [5,7]. Unlike in infants, episodes of clinical malaria in adults were not always accompanied by the presence of malaria parasites in thick smears [5].

Further immunological investigations on Nigerians infected with chloroquine resistant *Plasmodium falciparum* were carried out in two different part of Nigeria (Calabar, Southeastern Nigeria and Ibadan, Southwestern Nigeria). The results showed a higher prevalence of chloroquine resistant *Plasmodium falciparum* in Calabar when compared with Ibadan. It was also reported that chloroquine resistance or sensitivity to *Plasmodium falciparum* in Nigerians was based on differences in certain cell-mediated immunity since most of the humoral immune responses (except IgG3) were similar in chloroquine resistant and sensitive groups [8].

A slight diminution in the mean IgG3 concentration in the malaria-infected patients suggested the importance of IgG3 in control of malaria [9]. Other study provided further evidence for the restriction of immunosuppression in malaria-infected patients to some specific T and B-cell related functions [10]. Depressed leucocyte migration and phagocytosis in malarial subjects made them susceptible to secondary bacterial infections [11].

A study on experimental models of infections and observations in humans indicated that immune complexes (IC) play important role in the pathogenesis of nephropathies associated with malaria and that malarial IC might trigger a pathogenic sequence in which other mechanisms (perhaps autoimmune?) might later be involved [12].

2.2 Immunology of Malnourished Nigerian Children

The major findings on immune responses in malnourished children were (i) normal phagocyte bactericidal ingestion rates and but reduced phagocyte bactericidal digestion rate [13], (ii) significant reduction in the proportion of T lymphocytes but adequate synthesis of globulins, IgG, IgA and IgM in malnourished children following tetanus toxoid immunization [14], (iii) presence of a high molecular weight heat-labile substance (migrating in the alpha-2-macroglobulin region) in the serum of malnourished children which inhibited E- rosettes formation [15].

The impaired bactericidal activities, diminished antibody productions and apparent reduction of thymus derived lymphocyte proportions observed in malnourished children were reported to be some of the major causes of the higher incidence of infections in malnourished children. The depressed T lymphocyte number in malnourished children affected their ability to handle antigens such as measles virus in vivo [16].

2.3 Immunology of Nigerian Children with Urinary Schistosomiasis

Urinary schistosomiasis (USS) is a human parasitic disease caused by *Schistosoma haematobium* and its public health significance is often underestimated. Immunological studies on urinary schistosomiasis (USS) in this Immunology Unit established for the 1st time that Nigerian subjects with USS exhibited autoimmune phenomenon [17], have effective neutrophil phagocytosis [18] and adequate functions/levels of certain Complement factors [19]. Nigerian USS subjects have reduced malaria parasitemia, reduced bacteremia [20], normal renal functions and anthropometric indices [21] thus further supporting why USS is grouped among "neglected diseases". Different acute phase proteins were proposed to have diagnostic values in female genital schistosomiasis [22].

Epidemiological importance of immunological studies of USS patients was established. Treatment with Praziquantel, an antischistosomal drugs was observed to normalize the serum concentrations of IgG, IgA, CIC, caeruloplasmin, CRP and haptoglobin and % migration indices (using schistosome soluble egg antigen) demonstrated in untreated USS subjects [23]. Classification of USS into different severity groups was previously based on *Schistosoma haematobium* eggs per 10ml urine [24], which is inconsistent and unreliable. Based on studies from this Immunology unit, it was established that USS among Nigerians was in acute stage but not in chronic stage despite high egg count [25].

There was good evidence that schistosomal immunopathology results from deposition of immune complexes developed from reaction between schistosome antigens and host

antibodies [26]. It was established that IgM associated circulating immune complexes was involved in the pathogenicity of USS in Nigerian patients [23]. Apart immune complexes, deposition of eggs in various organs are also responsible for certain immunopathology of *Schistosoma* infection such as inflammation [22, 23], allergic reactions, anatomical complications and granuloma [27]. Study on USS in this Immunology Unit showed the presence of a serum inhibitory substance which prevented rapid formation of granuloma in schistosomiasis subjects. This could have prevented the development of nodules and eventual organ complication in mild schistosomiasis as in Nigerians with urinary schistosomiasis. This serum substance was a dialyzable, high molecular weight and heat sensitive glycoprotein which migrates with alpha 2-and gamma globulins [28].

Immunology is an interdisciplinary science whose methods are required for researches and investigations in a number of fields. Collaborative studies of this Immunology Unit with various Departments and Faculties provided the following information which is unavailable in this environment as follows:

2.4 Immunology of Pregnancy

- (a) Low birth weight babies (LBW) had depressed leucocyte motility/phagocytosis but normal levels/haemolytic functions of Complement factors compared with full term babies [29]. But preterm babies had reduced levels of complement factors and normal Complement haemolytic activities [29,30]. Thus, explaining increased susceptibility of LBW and pre-term babies to infections.
- (b) Mice infected with *Leishmania major* preferentially resolved the infection at the expense of losing the pregnancy. This was based on the levels of IL 4 and IFN gamma in the supernatant of lymphocytes from inguinal lymph nodes [31].
- (c) Abnormal humoral immune responses and bacterial infections were shown to be involved in the pathogenicity of pre-eclampsia [32] and recurrent abortion [33].
- (d) There was higher prevalence of malaria parasitemia but lower malaria parasite density in pregnant women than parturient mothers. Neutrophil phagocytosis, complement haemolytic activity and T-lymphocytes were reported to be the effector mechanisms that limit the parasitemia in pregnant women with asymptomatic malaria parasitemia [34]. The epidemiological implication of this study was that pregnant women served as reservoirs for spreading malaria parasites in the studied population.

2.5 Immunology of Ageing

Immunology of apparently healthy Nigerians have shown increased incidence of cancer and autoimmune diseases in the elderly. Lymphocyte subpopulations were found to be similar in all age groups but cellular immune functions declined with increasing age. Mean leukocyte migration decreased with rising age [35]. The mean tuberculin reaction diameter increased progressively between the ages of 6 and 40 years, and decreased by above 50 years of age. The numbers of B-cells, T-cells, null cells, helper T-cells and suppressor T-cells were the same in the different age groups. Also circulating immune complexes, C4 and auto-antibodies were raised with increasing age [36]. The mean values for C3 and Complement Factor B did not change significantly with age [37]. The study concluded that susceptibility to infection in old individuals could be reduced by modulating their immune responses [38]. It was also found that there was a general increase in IgG levels with advancing age especially in the first 20 years of life. IgA increased progressively with age from 1 to 50

years. The male IgM levels generally rose with increasing age while there was no significant elevation in female IgM values. Females had higher levels of IgG, IgA and IgM in the first 10-20 years of life after which the levels were either the same or higher in the males. A significant seasonal influence on IgA, IgG and IgM concentrations could not be demonstrated [39].

Immunoglobulin G was reported fall in value in the first few days of life to about 62% of the value in the last days of the neonatal period. There was however a gradual increase in the level of IgM to about double at the end of the neonatal period. IgA level remained relatively constantly low throughout this period. The effect of maternal education on the levels of immunoglobulins of their neonates was also investigated. There was a positive influence at the secondary educational level, affecting only the IgG and IgA [40]. Deficiencies of immunoglobulin classes were discovered in subjects living at high altitude.

A study of immunoglobulin allotypes in various Negro populations showed that their polymorphism was different from populations. This was particularly true for the alleles of the gamma 3 and alpha 2 loci. In comparison of the results determining Ig markers in different tribes from various African countries, the information lead to additional support for theories on the origin and migration of early African inhabitants [41].

2.6 Immune Responses in Sickle Cell Anaemia

The studies used immunological parameters to classify sicklers (HbSS individuals) into 3 groups: mild, moderate and severe. The severe HbSS group had the highest deranged immune responses. Neutrophil functions and percentage T-cells of mild and moderate HbSS individuals did not differ significantly from those of the control groups while marked impairment was observed in the severe group. Transferrin and haptoglobin were reduced while C - reactive protein and caeruloplasmin were elevated in HbSS individuals [42]. Complement regulators (C1 inhibitor and C3 activator) contributed to the susceptibility of HbSS to *Plasmodium falciparum* malaria [43].

2.7 Immune Responses in Human Immunodeficiency Virus (HIV) and Pulmonary Tuberculosis Patients

A study of Nigerians with HIV infection revealed an abnormally thick gamma bands alone or fusion of gamma band with beta band in some of the patients. Further analysis of the proteins showed elevated serum IgG, IgA, IgM, globulin, C-reactive protein and transferrin [44].

The conclusions drawn were:

- Elevated circulating immune complexes and nonspecifically raised immunoglobulin classes might be responsible for deranged immune responses in Nigerians with HIV infection [45].
- Different acute phase proteins were proposed to have diagnostic values in differentiating pulmonary tuberculosis patients on chemotherapy from newly diagnosed PTB patients.
- Plasma levels of C1 inh and C4 might be used to distinguish HIV severity [46].

2.8 Immune Studies on Breast-milk and Saliva

The most commonly used laboratory diagnostic procedures involve the analyses of the cellular and chemical constituents of blood. Whole saliva can be collected non-invasively, and by individuals with limited training. No special equipment is needed for collection of the fluid. Diagnosis of disease *via* the analysis of saliva is potentially valuable for children and older adults, since collection of the fluid is associated with fewer compliance problems as compared with the collection of blood. Further, analysis of saliva may provide a cost-effective approach for the screening of large populations [64].

It has been demonstrated that cigarette smoking reduces serum levels of immunoglobulins including IgG, IgA and IgM, suppresses cell mediated immune responses and damages lymphocytes [65], thus predisposing smoker to respiratory infections.

No significant differences were observed in salivary levels of the immunoglobulin classes when cigarette smokers with periodontitis were compared with cigarette smokers without periodontitis. Mean salivary levels of IgA and IgM were significantly lower in cigarette smokers with periodontitis when compared with non-smokers having periodontitis. Only IgM was significantly lower in cigarette smokers with periodontitis when compared with non-smokers without periodontitis. Salivary IgA and IgM levels were found to be significantly lower in smokers without periodontitis when compared with non-smokers having periodontitis. Reduced IgA and IgM levels were proposed to explain susceptibility of cigarette smokers to oral diseases or progression of periodontitis [47,48].

The effect of Human Immunodeficiency Virus (HIV) on the immune system is well documented however; its impact on the nutritional and immunological qualities of the breast milk is scarce. A preliminary data generated from our Immunology Unit reported raised transferrin in breast milk of HIV infected lactating mothers compared with HIV seronegative lactating mothers. Breast milk levels of albumin, pre-albumin and retinol binding protein were not significantly different in HIV negative and positive mothers [49].

Another study observed that breast milk levels of IgA, IgM, caeruloplasmin and complement factor IIIc were significantly elevated in HIV infected mothers compared with HIV uninfected mothers [50]. The study suggested that elevated breast milk levels of IgA, IgM and Complement Factor 3 might be to protect their infants through neutralizing HIV. Also, breast milk of HIV infected mothers had low total antioxidant capacity [51], thus suggesting that HIV-infected mothers who insist on breastfeeding their babies should complement breastfeeding with antioxidant rich supplements.

2.9 Lifestyle Factors and Immunity

The link between social factors and health has been the focus of many interdisciplinary studies. Immune system is under the influence of a number of factors which lifestyles are among these factors.

2.9.1 Exercise and physical activity

Exercise and physical activity has a generalized influence on the whole body. World Health Organization and the American Heart Association have previously advised a minimum of 30 minutes of physical activity for at least 5 days per week. A study reported that adults who

performed a moderate amount of physical activity also had better immune activity than others who led a sedentary life [52]. C-reactive protein was significantly increased while transferrin and haptoglobin were significantly reduced in subjects doing prolonged exercise when compared with sedentary subjects. In moderate exercise, haptoglobin was significantly reduced while the reduction in the levels of caeruloplasmin and transferrin were not statistically significant when compared with sedentary subjects. The mean level of CRP was significantly raised during prolonged exercise compared with controls or moderate exercise while the level of caeruloplasmin was significantly reduced in prolonged exercise compared with sedentary or moderate exercise. It was recommended that moderate exercises should be encouraged.

2.9.2 Alcohol and Cigarette smoking

Alcohol is a very common chemical in today's society and has been around for thousands of years. Excessive alcohol was found to damage immune system because alcohol reduces the white blood cell count and essential food like vitamins needed by immune cells. Nitric oxide, transferrin, total WBC count and neutrophils were significantly reduced while IgM was significantly raised in Nigerians that consume alcoholic beverages compared with the controls. The volume of alcohol consumed daily showed negative correlation with transferrin and total WBC [53,54]. The study indicated that alcohol adversely affected certain humoral immunological parameters and this may account for the susceptibility of alcoholics to infections.

Cigarette smoking weakens the immune system by depressing antibodies and immune cells. There is an association between smoking and the increased incidence of certain malignant diseases, respiratory infections and reduced essential nutrients. The mean values of antioxidant vitamins C and E were significantly lower while Nitric oxide was not significantly reduced in the smokers compared with non-smokers. The level of alpha-2-macroglobulin was significantly raised while caeruloplasmin was not significantly raised in smokers compared with non smokers. This study confirmed that inflammation is a common phenomenon in cigarette smokers and that significantly decreased levels of antioxidant vitamins C and E and raised level of caeruloplasmin might explain the development of cardiovascular diseases in cigarette smokers [55]. Other striking findings were second hand or passive smoking has equally adverse effect on health as active smoking [56] and that alcohol drinking had non-synergistic effects as cigarette smoking on health [57].

Plasma levels of IgG, IgM, CRP and A2MG were significantly raised while vitamins C and E were significantly reduced in active smokers compared with the controls. Plasma levels of CRP and A2MG were significantly raised while vitamins C and E were significantly reduced in passive smokers compared with the controls. Levels of CRP and antioxidant vitamins were similar in active and passive smokers. It was suggested from this study that exposure to passive cigarette smoke might cause oxidative stress and inflammation as active smoking [56]. Thus long time exposure to passive cigarette smoke might lead to pathologic conditions as active smoking and this may due to vitamins C and E deficiencies.

2.9.3 Skin-lighten cream users

The outermost skin layer (the epidermis) provides the first line of defense against pathogens. This skin layer is removed by skin lighten creams. Lightening of skin is practiced by black people at all ages, and in both sexes with higher prevalence in young, unmarried and educated women for fame, cosmetic purpose and also due to misconceptions about the

presumed superiority and desirability of fair skin. But the big disadvantage of the habit of skin lighten is that skin lightening creams cause disruption in the normal natural immunologic functions of the skin. The mean of neutrophil was significantly lower while the mean value of lymphocytes was higher in the users of skin lightening creams when compared with the controls. There was significantly increased diameter of skin reaction to Mantoux test in the users of skin lightening creams when compared with the controls. Skin prick test to environmental allergens also showed significantly increased reaction diameter with dog epithelia antigen in the users of skin lightening creams when compared with controls. Significantly higher proportions of the users of skin lightening creams were positive to GS2 cockroach antigen, standardized mite antigen and mouse epithelia antigen when compared with the controls [58].

The study showed that skin lightening creams caused disruption in the normal immunologic functions (Types I and IV hypersensitivity states) of the skin and certain haematological parameters. There is need for public awareness programs to enlighten the populace about the danger involved in the practice of skin lightening.

2.10 Immune Studies of Nigerians Occupational Exposed to Chemicals

Although scientists have known since the early 1900s that occupational exposure to certain chemicals can induce severe immune effects. This is further supported by the fact that human health is influenced by environment and that many diseases are caused or enhanced by environmental factors. Researchers in the field of immunotoxicology reported that certain chemicals can affect immunity, significantly increasing an individual's susceptibility to disease, in some cases causing hypersensitivity reactions, autoimmunity, or immunosuppression [59]. Others dispute this view, arguing that the evidence for immunotoxicity in humans is greatly overstated [60]. In one of our study, it was found that level of IgM was significantly raised while acute phase proteins (alpha-2 macroglobulin, caeruloplasmin and transferrin) and immunologically essential trace elements (Fe, Zn, Cu and Se) were not significantly different in cassava processor despite prolong exposure to cyanide chemical compared with un-exposed individuals [61]. The significantly elevated IgM observed might indicate complement activation by sublethal cyanide concentrations in the cassava processors. Therefore micronutrients supplementation in cassava processors is necessary. Also the use of Vitamin B₁₂ in the active form (methylcobalamin) is recommended for the cassava processors because cobalamin binds cyanide to reduce cyanide toxicity.

A study showed that metal toxicity is imminent in panel beaters, automobile mechanics and motor painters and that the metals involved vary with occupations. This raises the need for public awareness about the hazards of different occupations in order to enable these professionals take necessary precautionary measures [62]. Also, Ig classes were similar in petroleum attendance compared with controls [63]. Thus, supplementation with nutritionally essential trace metals and antioxidants was advocated to boost the immune system of these subjects.

Table of the summary of major researches in immunology laboratory in Ibadan, Nigeria

References	Subjects	Achievements
31	Pregnant mice	Raised IL-4 impaired the resistance of pregnant C57BL/6 mice to <i>L. major</i> infection.
74	Pregnant mice	Raised IFN-g was associated with reduced litter weight of <i>L. major</i> infected pregnant C57BL/6 mice especially those infected at late stage of pregnancy
66	Hepatitis B infection	Reduced transferrin and increased alpha-2 macroglobulin in Hepatitis B Virus carriers suggested active liver disease.
67	Diabetes mellitus	More derangement of humoral immunity in Type 2 diabetics compared with Type 1 diabetics probably due to hyperinsulinemia.
38	Ageing	Circulating immune complexes and C4 increased with age.
35	Ageing	Phagocyte function is unchanged in aging Nigerians.
36	Ageing	Autoantibodies contributed to increased prevalence of CICs in old individuals.
20	Urinary schistosomiasis	Adequate neutrophil phagocytic function in urinary schistosomiasis subjects (USS) explained the absence of clinical manifestations of bacterial and viral infections in these subjects.
23	Urinary schistosomiasis	The study concluded that IgM associated-CIC may be responsible for the immunopathology of chronic schistosomiasis.
18	Urinary schistosomiasis	LMIF assay using schistosome antigen(s) has epidemiological value in schistosomiasis.
19	Urinary schistosomiasis	Immunological findings suggested that urinary schistosomiasis in Nigerian subjects was in the acute stage.
22	Urinary schistosomiasis	The results indicated that USS or pregnancy changes different aspects of humoral immunity, thus the co-existence of pregnancy and <i>S. haematobium</i> infection may influence each other.
43	Urinary schistosomiasis	The switch of complement activation pathway from alternative type in USS subjects to classical type in malaria subjects may explain the lower malaria parasite densities often found in children harbouring <i>Schistosoma haematobium</i> parasites.
69	Auto-immune diseases	The presence of auto-antibodies to DNA is not a reliable diagnostic index for auto-immune phenomena.
68	Auto-immune diseases	The presence of auto-antibodies to DNA is not a reliable diagnostic index for auto-immune phenomena.
17	Auto-immune diseases	Soluble immune complexes (SIC) and anti-DNA antibodies were induced by antigens from eggs of <i>S. haematobium</i> and that both SIC and anti DNA antibodies were involved in the pathology of USS.
70	Sickle cell anaemia.	CH50, C3, C4 and Bf did not correlate with either the number of crises or complications in sickle cell anaemia patients.
42	Sickle cell	Transferrin and CRP were suggested as plasma proteins

	anaemia.	worthy of further evaluation as indicators of severity in homozygous sickle cell disease.
71	Sickle cell anaemia.	Markedly raised levels of IgG and IgG3 may be predictive of severity in sickle cell anaemia.
3	Malaria in neonates	The study indicated that haemoglobin genotype contributed to protection of newborn against malaria parasitemia.
5	Malaria in neonates	The fairly rapid increase in parasite rate and density after two months of age was indicative of the decrease in protection after the first 2-3 months of life.
6	Malaria in neonates	The finding of an active antibody response to malarial antigens in infancy encouraged the hope that malaria vaccine administered early in life may accelerate the development of naturally acquired immunity and thus protect the population most at risk.
73	Acute lymphocytic leukemia	Immunoglobulin G levels showed a significant positive correlation with survival in ALL patients.
40	Immunoglobulin levels	This study reported a positive influence at the secondary educational level on IgG and IgA.
39	Immunoglobulin levels	Females had higher levels of IgG, IgA and IgM in the first 10-20 years of life after which the levels were either the same or higher in the males.
72	Immunoglobulin levels	Serum levels of these immunoglobulins are of limited value in either the diagnosis of asthma or in the grading of its severity.
40	Immunoglobulin levels	There were no significant differences between the mean IgA and IgM levels of newborns in different gestational age groups. There was no detectable level of IgD in the cord sera.
13	Malnutrition	The study suggested that nutritional repletion corrects the impaired cellular responsiveness in malnourished patients.
16	Malnutrition	Depressed T lymphocyte number in malnourished children affected their processing of antigens such as measles virus <i>In vivo</i> .
47, 48	Periodontitis	The study suggested that reduced salivary immunoglobulin level of IgM might be involved in the pathogenesis of oral diseases in cigarette smokers and that IgA could be used as a screening tool for periodontitis.
30	Neonates	Percentage T cell, C3, C5, %NBT and %C.I were lowest in low birth weight babies but % B cell was lowest in full term babies while normal birth babies had least %M.I. The study suggested that gestational age and birth weight affect different aspects of immune response.

3. MISCELLANEOUS STUDIES

Immunological analysis of saliva was found to be useful for the diagnosis of oral and systemic hereditary disorders, autoimmune diseases, immune suppression, malignant and infectious diseases, and endocrine disorders, as well as in the assessment of therapeutic

levels of drugs and the monitoring of illicit drug use [64, 65]. In other studies, serum immunoglobulin classes and acute phase proteins were found to have limited values in diagnosis of diabetes mellitus and monitoring development of hepatocellular carcinoma among Nigerians [66,67]. Low circulating IgA levels in Nigerians with joint pains was reported to be caused by depressed thymic activity, development of autoimmunity or utilization in immune complex formation [68]. The mean concentration of soluble immune complexes was significantly higher in patients with joint pains than in the apparently healthy subjects [68] and the positivity rates of auto-antibodies to DNA in these subjects and those without joint pains were comparable [69]. A study reported no significant differences in the levels of CH50, C3 and C4 in sickle cell disease patients compared with controls, and that these parameters and Complement Factor B (Bf) did not correlate with either the number of crises or complications [70]. In contrary, IgG, IgA, IgM, IgG1 and IgG3 levels were significantly raised in the sickle cell disease patients when compared with the controls. Total IgG concentration and level of the IgG3 subclass showed significant positive correlation with frequency of crisis and severity score. Markedly raised levels of IgG and IgG3 were found to be predictive of severity in sickle cell anaemia [71]. Mean IgG and IgA levels in the asthmatics were not significantly different from those in the controls. Conversely, mean IgM values in female controls and all the controls were significantly higher than those in their asthmatic counterparts. The study found no relationship between severity of asthma and the mean levels of the various immunoglobulins [72]. Hypoimmunoglobulinaemia was observed to contribute to the aetiology of acute lymphoblastic leukemia (ALL) that IgG levels showed a significant positive correlation with survival ALL patients. The adverse effect of reduced immunoglobulin G on the prognosis of acute lymphoblastic leukemia was related to compromised immunity in ALL patients. Pregnancy was aborted in pregnant mice so as to eliminate intracellular *L. major* infection as a result of cytokine switch [74].

4. CONTRIBUTION OF IMMUNOLOGY LABORATORY TO QUALITY OF LIFE

With more knowledge of how the immune defense system responds during disease conditions, the findings had lead to enhanced treatment and better quality of life for those suffering these diseases. The Immunology laboratory is improving manpower because researchers from other institutions/countries learn available basic techniques in immunology and few of them analyse their research samples in this laboratory.

The international community got exposed to strengths of immunology scenario in this Nigerian institution through presentations in conferences and publications in reputable journals. This has lead to increase in collaborations in terms of research and exchange programmes, which continue to rise till date.

Despite above, immunology is one very important field that needs to grow at faster pace in the area of disease burden, thus there is a rapid need to improve infrastructure and to train people in the area of immunology so that local diseases and their remedies are better and quickly addressed.

5. FUTURE INVOLVEMENT

Immunology is a flowering science where immunological techniques are required for a wide variety of investigative work in diagnosis and research. There have been rapid advances in methodology in tune with the status of modern immunology as a highly evolved molecular and cellular science.

Immunology Unit of University of Ibadan, Nigeria has put research results and methodologies into clinical applications and diagnostic uses. Apart from our immunological investigation in a number of fields (microbiology, in biochemistry and molecular biology, endocrinology, toxicology, haematology, clinical medicine), the Unit is presently extending investigations in allergy/hypersensitivity, household air pollution study, breast cancer and histocompatibility cross-matching. The Unit is also investigating the immunological basis of vaccine efficacy in children and elders with different diseases. Moreover, the roles of microbiomes, DNA methylation and inflammation in cancer progression are being investigated.

6. CONCLUSION

Immunology in Nigeria is in a phase of expansion and it is unique in that it provides a constant stream of new knowledge from which novel diagnostic tests and therapies eventually emerge for use in clinical practice. It is obvious from present review that most previous studies in this Immunology Unit concentrated on infectious diseases with little attention given to immuno-toxicology or immune-endocrine interaction. Studies on the functions of leucocytes, molecular analysis of the immune system and its genetics are becoming increasingly important and will be put in the panel of investigations by the Unit to close the gaps in research and clinical activities.

7. DEDICATION

This review is affectionately dedicated to Past Professors (Houba V, Osunkoya B.O, Williams I.A and Salimonu L.S) of Immunology, Department of Chemical Pathology, University of Ibadan, Nigeria.

COMPETING INTERESTS

Author has declared that no competing interests exist.

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