

## Dynamics of Immune and Gene Therapy in Nigeria: A Narrative Review of Related Studies

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### Abstract

**Background:** In recent times, there has been a huge success with respect to the application of immune and gene therapy. However, little is known about its state in Nigeria.

**Objectives:** The study narratively reviewed the dynamics and distribution of Immune and Gene therapy utilization and related studies in Nigeria from 1980 to 2019.

**Methods:** The study utilized narrative review to explain the state of Immune and Gene therapy in Nigeria. Literature was retrieved from computerized databases using appropriate search terms. Data obtained was entered into an Excel Worksheet and summarized using descriptive statistics namely frequency and percentages.

**Results:** Overall, 21 publications from a total of 6110 was selected (0.03% selection rate) and based on geographical region, the South-Western had the highest distribution (33.3%).

**Conclusion:** Some studies on Immune and Gene therapy management activities have been carried out in the country. However, the level of utilization, status, complexity, and distribution of studies are still at the developmental stage and the potentials remain grossly untapped .

**Keywords:** Immune Therapy; Gene Therapy; Narrative Review; Trends; Nigeria

## Introduction

Immune therapy also referred to as immunotherapy, biologic therapy, or biotherapy, “is the treatment of diseases by activating or suppressing the immune system” [1]. It aims at improving the body’s defense mechanism. In 1890, William Coley, a New York surgeon treated a girl with sarcoma via immune therapy, using a bacterium known as Coley’s toxin. It has become a focus for the treatment of most cancers [2]. Gene therapy, on the other hand, “is the therapeutic delivery of nucleic acid intracellularly to treat diseases and is known as human gene therapy” [3]. It was first conceptualized in 1972. However, the first recorded and approved gene therapy research took place in the US, on September 14, 1990, at the National Institute of Health (NIH), under the direction of William French Anderson where a four-year-old girl, Ashanti DeSilva, received treatment for Adenosine deaminase (ADA) deficiency, a genetic disease which caused Severe Combined Immunodeficiency (SCID), leaving the patient prone to diseases [4]. Gene therapy may be somatic or germline and these modified genes were introduced via techniques like electroporation, sonoration, polymerase chain reaction (PCR), nanoparticles and gene gun [5].

Both immune and gene therapy are novel approaches to treating a variety of genetic diseases and cancers. Successes have been recorded in the treatment of Prostate cancer, Lipoprotein lipase deficiency, Severe Combined Immunodeficiency (SCID), Breast cancer to mention a few [6]. However, some drawbacks which may dissuade their usage include mutagenesis, immune response, cost, numerous biological barriers, and some ethical issues attached. Nevertheless, active research in cell and gene therapy at both academia and industry levels continuously provides fresh insight that promises to bring these potentially potent therapies to our doorstep [7].

Presently, there have been tremendous successes with immune and gene therapy. However, no reported breakthrough in the literature of success in immune and gene therapy in developing countries like Nigeria. As a result, developing countries are lagging in this new trend of therapeutics. Hopefully, by the next decade, they should be able to join the League of Nations in applications of these methods for the treatment of diseases [5]. This study reviewed the dynamics of Immune and Gene therapy in Nigeria from 1980 to 2019.

## Methods

### Study area

The study covered published studies related to immune and gene therapy in Nigeria.

### Review question

What is the extent of Immune and Gene therapy in Nigeria?

### Study population and type of study included

We used studies which passed the eligibility criteria and were found in Google Scholar, PubMed, and African Journals Online.

### Eligibility criteria:

### Inclusion criteria:

- Studies published in English language
- Studies related to immune and/or gene therapy carried out in Nigeria
- Studies carried out between 1980 and 2019
- Studies that provide information to help understand immune and gene therapy.

### Exclusion criteria:

- We excluded all studies related to the subject, covering the study period, and published in English Language, but with invalid or inconclusive methods or data

### Study design

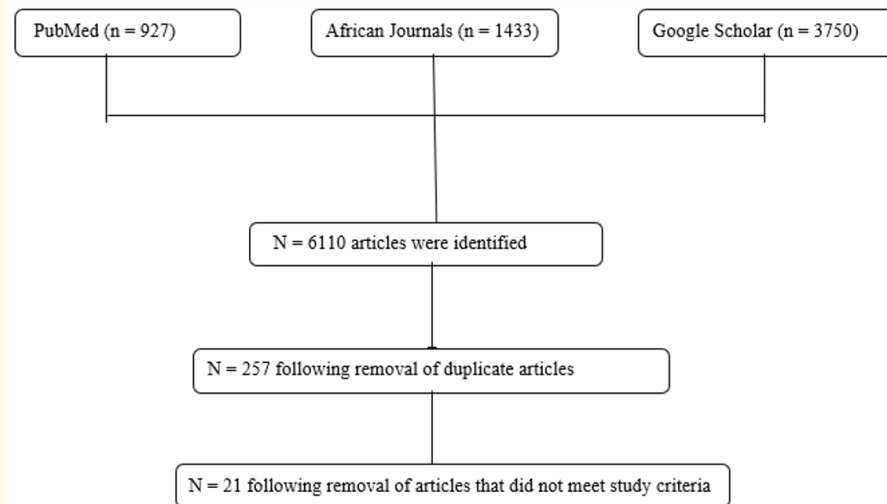
The study was a narrative overview of Immune and Gene therapy studies in Nigeria.

### Information source

The search utilized Google Scholar, PubMed, and African Journals Online.

### Articles search process

We searched Google Scholar, PubMed, and African Journals Online for studies and articles on Immune and Gene therapy in Nigeria published between 1980 and 2019. Relevant studies like ‘immune therapy in Nigeria’, ‘gene therapy in Nigeria’, ‘trends of immune and gene therapy in Nigeria’, were additionally searched. A total of 6110 articles were obtained relating to immune and gene therapy: 3750 from Google scholar, 927 from PubMed and 1433 from African Journals Online (Figure 1). These articles were assessed for eligibility.



**Figure 1:** Flowchart of the study articles selection process.

### Study articles selection process

A total of 6110 articles were obtained relating to immune and gene therapy: 3750 from Google scholar, 927 from PubMed, and 1433 from African Journals Online. These were assessed based on the eligibility criteria. Duplicate articles were removed and on further screening, a total of 21 articles were used for the review.

### Data analysis

For the bibliographic analysis, data extracted from the selected articles were entered into a spreadsheet for statistical analysis (Microsoft Office Excel Windows 10 version). The variables registered for each article were: author, year of publication, geopolitical zone, study design and sample size. Descriptive analyses of the relevant study variables were summarized in tables and figures.

Results

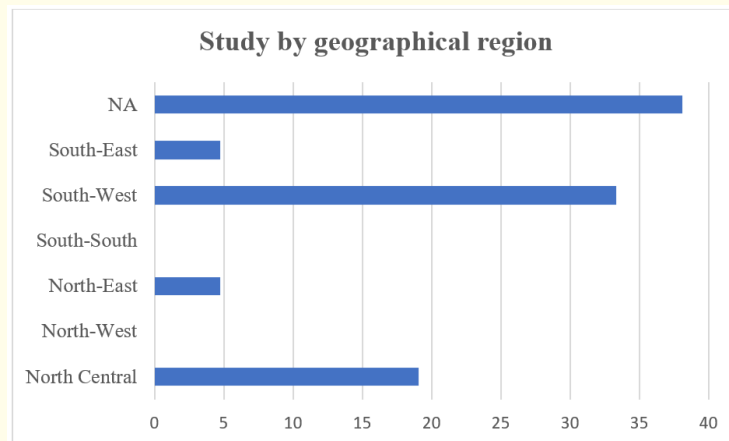
Author	Title	Year of Publication	Geopolitical Zone	Study Design	Sample Size
8	Inter-individual variation in imatinib disposition: Any role for prevalent variants of CYP 1A2, CYP 2C8, CYP 2C9, and CYP 3A5 in Nigerian CML patients?	2018	South-West	Hospital-based Prospective Cohort Study	42
9	Assessment of Markers of Antimalarial Drug resistance in <i>Plasmodium falciparum</i> isolates from pregnant women in Lagos, Nigeria	2016	South-West	Case Series Report	54
10	Hormone receptor expression status of epithelial ovarian cancer in Ibadan, South-Western Nigeria	2017	South-West	Prospective Cohort Study	115
11	A rare case of Lupus Vulgaris in a Private Tertiary health facility in South-Western Nigeria	2018	South-West	Case Report	1
12	Post-neonatal tetanus in University of Maiduguri Teaching Hospital, North-Eastern Nigeria	2013	North-East	Hospital-based Prospective Cohort Study	39
13	Monoclonal antibodies: A review of therapeutic applications and future prospects	2017	Not Applicable	Review	Not Applicable
14	The anti-bacterial potentials of a phage-therapy: A review	2011	North-Central	Review	Not Applicable
15	Genomic Interventions in Medicine	2018	Not Applicable	Review	Not Applicable
16	Gene therapy in the developing countries	2015	Not Applicable	Review	Not Applicable
17	Presenting features and treatment outcomes of chronic lymphocytic leukemia in a resource poor Southern Nigeria	2019	South-East	Case Report	97
18	Biotechnology: Advances and prospects for sustainability in Nigeria	2000	North-Central	Review	Not Applicable
19	Genetic Diversity of the <i>Plasmodium falciparum</i> Glutamate-Rich Protein R2 Region	2018	South-West	Prospective Cohort Study	270
20	Modified T-cells (using TCR and CTAs), Chimeric Antigen Receptor (CAR) and other molecular tools in recent gene therapy	2017	Not Applicable	Review	Not Applicable
21	Current strides in AAV-derived vectors and SIN channels further relieves the limitations of gene therapy	2018	Not Applicable	Review	Not Applicable
22	High prevalence of dihydrofolate reductase gene mutations in <i>Plasmodium falciparum</i> parasites among pregnant women in Nigeria after reported use of Sulfadoxine-Pyrimethamine	2018	South-West	Cross-sectional Retrospective Study	200

23	Gene therapy for sickle cell disease	2012	Not Applicable	Review	Not Applicable
24	Immunotherapy with <i>Mycobacterium vaccae</i> as an addition to chemotherapy for the treatment of pulmonary tuberculosis under difficult conditions in Africa	1995	North-Central	Single Blind Randomized placebo-controlled trial	180
25	Interplay of post-translational modification and gene therapy	2017	Not Applicable	Review	Not Applicable
26	Rectal cancer: Pattern and outcome of management in University of Ilorin Teaching Hospital, Ilorin, Nigeria	2010	North-Central	Prospective Cohort Study	36
27	Renal cell carcinoma in a semi-urban population of South-Western Nigeria	2017	South-West	Retrospective Review	51
28	Gene therapy, Physiological applications, Problems and Prospects - A review	2019	Not Applicable	Review	Not Applicable

**Table 1:** Evidence-based table of the characteristics distribution of selected study.

S/N	Period of publication of study	Number of Articles Published n (%)
1.	≤ 2000	2 (8.7)
2.	2001-2010	1 (4.3)
3.	2010-2019	18 (78.3)
4.	Total	21 (100)

**Table 2:** Periodic distribution of the articles.



**Figure 2:** Geographical spread of study.

NA = Not Applicable, i.e. no specific area of study for the reviews.

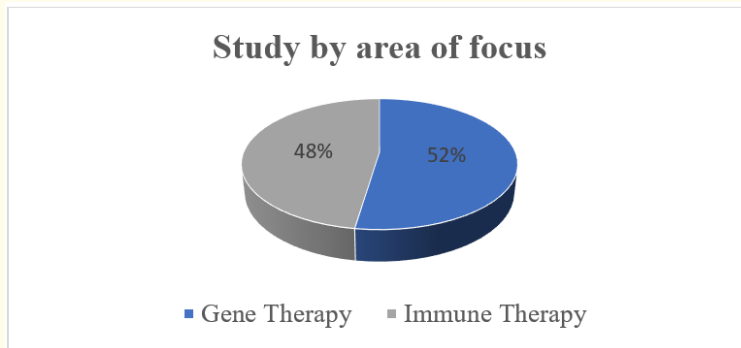


Figure 2: Study by area of focus.

### Discussion

The study revealed a high incidence of non-experimental studies. Thus, it can be inferred that the practical application of immune and gene therapy has not been fully integrated into the healthcare system of developing countries like Nigeria. The delay in the application of these therapies in Nigeria could be attributed to the time lag from the 70s when gene therapy was conceptualized to the 90s when it was actualized due to some factors such as ethical considerations, cost, and other factors. Presently, gene therapy studies focus on the discovery of resistant genes rather than its application as a tool for treatment. However, this has led to the improvement in chemotherapy by identifying genes that mutate slowly and seeking for drugs that act on them, thereby preventing resistance [9] and also understanding genetic polymorphism which helps in vaccine production to target the active sites e.g. in *Plasmodium falciparum* which remains a burden to the country [19]. Recently, phage-therapy is a growing area of research due to the ubiquity of bacteria [14].

Immune therapy dates back to the development of Coley’s toxin, a mixture of *Streptococcus pyogenes* and *Serratia marcescens*, used in the treatment of sarcoma in the 18<sup>th</sup> century [29] but most times used with chemotherapy. In Nigeria, success was seen in the use of *Mycobacterium vaccae* in the management of pulmonary Tuberculosis, although a major limiting factor for application was the lack of culture facilities [24]. Vaccination, another form of immune therapy practiced in the country has yielded positive results in the prevention of several diseases such as cervical cancer. The outbreak of tetanus in North-Eastern Nigeria could have been combated if the immunization schedule was strictly adhered to [12]. In 2002, the United States FDA approved the use of monoclonal antibodies (mAbs) in the management of cancers, leading to an exponential increase in its production [30]. In Nigeria, Imatinib (a mAbs) has been used successfully in managing Chronic Myeloid Leukemia (CML), though some patients have developed resistance due to some genetic variations [8]. Levamisole has been used as an adjuvant immunotherapy in the management of rectal cancer, though the success rate was not as high as surgery. Hence, surgery remained the mainstay of management after the research carried out in Ilorin, Nigeria [26].

Concerning geographical region, studies obtained from the southwest of the country have a higher frequency, although reasons for this was not clear. Very few studies have been carried out in the southeast and North-Eastern regions at the same rate. However, there was no record in the south-southern and North-Western regions. In addition, more studies were carried out on immune therapy than gene therapy. This is quite understandable as the era of immune therapy dates earlier than gene therapy. However, there have been more applications and uses in recent times than in the past. Therefore, more interest should be on gene therapy as well.

Immune and gene therapy are novel areas of study gradually being incorporated into the healthcare system of Nigeria. This may have contributed to the low incidence of studies. There were fewer studies in immune and gene therapy in past decades in Nigeria. However, it increased over time signifying gradual interest in this area of study. Although it may not be feasible due to certain constraints, there will be marked improvement and opportunities in this growing area of interest. Recently, the theoretical aspects have been added to the different school curriculum with minimal/no practical backing. Hopefully, the interest of students in this field will increase, opening more areas of research

### Conclusion

Although the application of immune and gene therapy has been used to cure diseases formerly considered incurable, more studies should be encouraged to translate the theory into practice and increase the incidence scope, and distribution of the studies. Immune and gene therapy and their applications are currently at the developmental stage in Nigeria. They are under-utilized, and the related studies studies are poorly distributed across the regions of the country.

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### Conflict of Interest

The authors have no conflict of interest to declare.

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