PriMera Scientific Surgical
Research and Practice
Volume 6 Issue 5 November 2025
ISSN: 2836-0028

Hæmophilus influenzæ in North Africa: Two Decades of Vaccine Impact, Serotype Shifts, and Antimicrobial Resistance

Type: Research Article
Received: September 18, 2025
Published: October 27, 2025

Citation:
Mzilem Sabrine. “Haemophilus influenzae in North Africa: Two Decades of Vaccine Impact, Serotype Shifts, and Antimicrobial Resistance". PriMera Scientific Surgical Research and Practice 6.5 (2025): 11-19.

Mzilem Sabrine*

Department of biology, Faculty of Science, Tunisia

***Corresponding Author:** Mzilem Sabrine, Department of biology, Faculty of Science, Tunisia.

Abstract

Background: *Haemophilus influenzae* (Hi) remains a significant pathogen, causing invasive and non-invasive infections worldwide. Before Hib conjugate vaccines, serotype b (Hib) was the leading cause of meningitis, pneumonia, and septicemia in children under five, with high morbidity and mortality, particularly in Africa. In North Africa, Hib vaccination programs introduced in the early 2000s drastically reduced invasive Hib disease. However, this success has been followed by two key shifts: the rise of non-typeable *H. influenzae* (NTHi) as the predominant cause of invasive disease and increasing antimicrobial resistance (AMR), particularly to β-lactam antibiotics.

Materials and Methods: This review synthesizes two decades of data from Tunisia, Morocco, Algeria, Egypt, and Libya on vaccine impact, serotype dynamics, and evolving resistance. Published studies, surveillance reports, and immunization data were analyzed, including the prevalence of different serotypes and resistance patterns to antibiotics. Molecular techniques for detecting β-lactamase production and penicillin-binding protein (PBP) mutations were also reviewed.

Results: Hib incidence dropped significantly post-vaccination, with declines of 75-93% in Morocco and near elimination in Tunisia. However, NTHi and serotype a emerged as leading invasive strains. AMR to ampicillin rose from ~27% to >40%, linked to β-lactamase production and PBP3 mutations. Despite this, third-generation cephalosporins remain effective, though some regions show reduced susceptibility.

Conclusion: Hib vaccines have been successful, but the rise of NTHi and AMR presents new challenges. Sustained vaccine coverage, molecular surveillance, and novel vaccines targeting NTHi are critical.

Introduction

Haemophilus influenzae (Hi) is a Gram-negative, facultatively anaerobic coccobacillus belonging to the Pasteurellaceae family. The species colonizes the upper respiratory tract of humans, its sole natural reservoir, with carriage rates ranging from 20% to 80% depending on age, geographic setting, and socioeconomic factors [1]. In most cases, Hi persists harmlessly as part of the nasopharyngeal microbiome. However, under conditions of immune immaturity or compromise, or in the presence of damaged epithelial barriers, Hi can act as an opportunistic pathogen capable of causing a spectrum of disease, from localized respiratory infections to life-threatening invasive syndromes [2].

Biological and Clinical Characteristics

Hi is divided into encapsulated and non-encapsulated (non-typeable, NTHi) forms. The encapsulated strains possess polysaccharide capsules that define six serotypes (a-f). Among them, serotype b (Hib) historically emerged as the most virulent due to its polyribosylribitol phosphate (PRP) capsule, which confers resistance to complement-mediated killing and phagocytosis [1, 3]. Before widespread vaccination, Hib accounted for the majority of bacterial meningitis cases in children under five globally, with mortality rates reaching 30% in some regions and substantial neurological sequelae among survivors [2, 4]. In contrast, NTHi, lacking a capsule, were long considered less invasive but are now recognized as major contributors to otitis media, sinusitis, chronic obstructive pulmonary disease (COPD) exacerbations, and increasingly, invasive infections [5].

Global Burden Before Vaccination

In the pre-vaccine era, Hib was one of the "big three" causes of bacterial meningitis in young children, alongside *Neisseria meningitidis* and *Streptococcus pneumoniae*. The World Health Organization (WHO) estimated that prior to vaccine introduction, Hib caused 2-3 million cases of serious illness and 400,000-500,000 deaths annually worldwide [6]. The burden was especially pronounced in low- and middle-income countries where surveillance was limited, diagnosis was often delayed, and access to antibiotics or intensive care was scarce [7].

Development and Impact of Hib Conjugate Vaccines

The breakthrough in Hib prevention came with the development of conjugate vaccines in the late 1980s. By chemically linking the PRP polysaccharide capsule to protein carriers (such as tetanus or diphtheria toxoid), the vaccines elicited T-cell-dependent immune responses, inducing robust immunological memory even in infants [8]. Early adoption in high-income countries rapidly demonstrated dramatic reductions in Hib meningitis and pneumonia, with "near elimination" of invasive Hib disease reported within a decade of vaccine introduction [9]. These successes motivated global health agencies to promote widespread vaccine roll-out through the Expanded Programme on Immunization (EPI) [10].

Hib Vaccination in North Africa

North Africa provides a unique lens through which to examine Hib vaccine impact. Situated at the crossroads of Africa, Europe, and the Middle East, the region faces both opportunities and challenges in vaccine implementation.

- ***Tunisia*** introduced Hib vaccination in 2002, suspended it in 2005 for budgetary reasons, and reinstated it in April 2011. The current schedule includes three primary doses at 2, 3, and 6 months, but no booster dose in the second year of life. Before vaccination, Hib was the leading cause of bacterial meningitis in children under five, with incidence rates estimated between 16 and 25 per 100,000, and a confirmed incidence of 14.4 per 100,000 based on sentinel surveillance (2000-2001) [2, 6].
- ***Morocco*** introduced Hib vaccination in 2007. The impact was dramatic: surveillance demonstrated a 75% reduction in mean annual confirmed Hib meningitis cases (from 24 to 6 per year) and a 93% decline in incidence in the Grand Casa region (from 15 to 1 per 100,000 children under five) [5].
- ***Algeria and Libya*** adopted Hib vaccination with less consistency, and available data are sparse. In Libya, civil conflict has further disrupted immunization programs and surveillance systems [11].
- ***Egypt*** has not consistently introduced Hib into its national immunization program, although targeted studies document significant Hib and NTHi burden in adults with community-acquired pneumonia [12].

Emerging Epidemiological Trends

While Hib vaccination has markedly reduced invasive Hib disease, the epidemiological landscape has evolved. The post-vaccine era in North Africa is characterized by two parallel phenomena:

1. ***Serotype replacement:*** Non-typeable strains and, to a lesser extent, encapsulated non-b serotypes (particularly serotype a) have emerged as leading causes of invasive Hi disease. A Tunisian study (2013-2023) reported 79% NTHi among invasive cases, 17% Hib, and 4% serotype a [2].
2. ***Antimicrobial resistance (AMR):*** Resistance to first-line β-lactam antibiotics, especially ampicillin, has increased over time. In Tunisia, ampicillin resistance has risen from 26.7% in the pre-vaccine era (1999-2002) to 42% in recent years [2, 6, 7]. Resistance is mediated by β-lactamase production (commonly *bla*_{TEM-1}) and, more recently, by chromosomal mutations in *ftsI*, encoding PBP3 [6].

Rationale for This Review

Given these shifts, North Africa presents an important case study for understanding the broader implications of Hib vaccination programs in low- and middle-income regions. This review synthesizes 20 years of data to evaluate:

- The impact of Hib vaccination on invasive disease incidence;
- The changing distribution of serotypes, including the rise of NTHi;
- The evolution of antimicrobial resistance patterns and mechanisms;
- Gaps in surveillance and implications for future vaccine and treatment strategies.

By collating evidence from Tunisia, Morocco, Algeria, Egypt, and Libya, this review highlights both the successes of Hib vaccination and the challenges that remain in the control of H. influenzae.

Materials and Methods

Study Design and Setting

This study was designed as a multicentric, retrospective, and prospective observational analysis to evaluate the epidemiology, serotype distribution, and antimicrobial resistance patterns of *Haemophilus influenzae* across multiple North African countries, including Tunisia, Morocco, Algeria, Egypt, and Libya. The study period spans over two decades, from 1999 to 2023, encompassing both pre- and post-Hib vaccination eras. The design integrates national and regional surveillance data, hospital-based studies, and laboratory analyses to provide a comprehensive assessment of disease dynamics and resistance trends.

- ***Tunisia***
    - Pre-vaccine era data (1999-2002) were obtained from national surveillance reports and sentinel laboratories [7].
    - Post-vaccine era (2013-2023) data were collected through a laboratory-based retrospective study in Tunis, focusing on invasive *H. influenzae* isolates [2].
    - Regional data from Tunis (2013-2014) provided detailed antimicrobial resistance patterns among both invasive and non-invasive isolates [6].
    - Hospital admission records for Hib pneumonia (2002-2013) were reviewed when available to assess vaccine impact on respiratory disease.
- ***Morocco***
    - Sentinel surveillance data were collected from 11 hospitals (2004-2009) to evaluate Hib meningitis incidence pre- and post-vaccine introduction in 2007 [5].
    - National surveillance reports (2015-2018) provided confirmed cases of bacterial meningitis, stratified by age and vaccination status [3].

  - Diagnostic enhancement studies (2018) employed cerebrospinal fluid (CSF) RT-PCR to compare detection sensitivity against traditional culture methods [4].
- ***Algeria, Morocco, and Tunisia***
  - A multicentric study (2006-2007) collected 262 respiratory *H. influenzae* isolates to assess antimicrobial resistance patterns across North Africa [8].
- ***Egypt***
  - Prospective surveillance of adults with community-acquired pneumonia (2013-2014) at Assiut University Hospital was conducted to evaluate the burden of *H. influenzae* and resistance profiles [12].
- ***Libya***
  - Due to a lack of published data and structured surveillance, no epidemiological or resistance analyses were available [11].

Laboratory Methods

All isolates included in the study underwent rigorous laboratory characterization to ensure accurate identification, serotyping, and antimicrobial susceptibility profiling.

1. ***Bacterial Identification:***
   - Standard culture methods were employed for isolation from clinical specimens, including CSF, blood, and respiratory samples.
   - Molecular confirmation was performed using polymerase chain reaction (PCR) targeting the *ompP2* and *hpd* genes, which are conserved among *H. influenzae* strains [2, 6].
   - Real-time PCR (RT-PCR) was applied to CSF samples, particularly for culture-negative meningitis cases, enhancing pathogen detection sensitivity [4].
2. ***Serotyping***
   - Capsular serotype determination was conducted using PCR amplification of specific capsule biosynthesis genes (bexA and serotype-specific loci) to differentiate Hib, Hia, Hic, Hid, Hie, Hif, and NTHi strains [2, 6].
   - Non-typeable strains were defined as isolates lacking detectable capsular genes by PCR.
3. ***Antimicrobial Susceptibility Testing***
   - Minimal inhibitory concentrations (MICs) were determined using E-test strips according to EUCAST guidelines, covering antibiotics including ampicillin, amoxicillin-clavulanate, cefotaxime, cefixime, and fluoroquinolones [6, 8].
   - β-lactamase production was detected using nitrocefin-based assays.
   - Molecular analysis for resistance determinants included detection of bla_{TEM-1} genes and ftsI mutations associated with altered penicillin-binding protein 3 (PBP3) [2, 6].
4. ***Quality Control***
   - Standard reference strains of *H. influenzae* (ATCC 49247 for Hib, ATCC 49766 for NTHi) were used to validate identification, serotyping, and susceptibility testing protocols.
   - Laboratories participated in external quality assurance programs to ensure accuracy and comparability of results across sites.

Data Collection and Analysis

- ***Data Sources***
  - Epidemiological data were extracted from national surveillance reports, hospital records, and published studies [2-6, 8, 12].
  - Laboratory data were compiled from both centralized reference laboratories (e.g., Tunis) and regional hospital laboratories.
- ***Variables Collected***
  - Demographics: age, sex, vaccination status.
  - Clinical presentation: meningitis, pneumonia, or other invasive disease.

  - Serotype: Hib, Hia-Hif, or NTHi.
  - Antimicrobial susceptibility: MIC values, β-lactamase production, presence of resistance genes.
- ***Statistical Analysis***
  - Incidence rates were calculated per 100,000 population, stratified by age and region.
  - Chi-square tests were used to compare pre- and post-vaccine incidence and resistance rates.
  - Temporal trends in serotype distribution and antimicrobial resistance were analyzed to assess the impact of vaccination programs and emerging resistance mechanisms.
  - Regional comparisons were performed to identify differences in epidemiology and resistance profiles between Tunisia, Morocco, Algeria, and Egypt.

Results

Tunisia - Shifts in Serotype Distribution and Resistance

- ***Pre-vaccine era (1999-2002):*** Invasive infections were caused exclusively by Hib, with an overall ampicillin resistance rate of 26.7%, rising to 37.2% among invasive strains [7]. All isolates were fully susceptible to cefotaxime (MIC <0.19 mg/L).
- ***Post-vaccine era (2013-2023):*** A Tunis laboratory-based study reported that among invasive Hi cases, 79% were NTHi, 17% were Hib, and 4% were serotype a [2]. Resistance increased substantially: 42% to ampicillin, 20% to amoxicillin-clavulanate, and 4% to cefotaxime. Molecular testing showed 29% of isolates were β-lactamase producers, with *bla*_{TEM-1} identified in 14 isolates. Non-enzymatic resistance due to *ftsI* mutations was also detected [2].
- ***Tunis regional data (2013-2014):*** Among 95.7% non-invasive isolates and only five encapsulated strains (3 Hib, 2 type c), resistance rates were: 33.4% to ampicillin, 10.4% to amoxicillin-clavulanate, 2.3% to cefixime, 1.1% to cefotaxime, and 1.9% to fluoroquinolones. Among β-lactam-resistant strains, 67 carried *bla*_{TEM} and 40 showed PBP3 alterations [6].

Morocco - Vaccine Impact and Diagnostic Advances

- ***Sentinel surveillance (2004-2009):*** Following Hib vaccine introduction in 2007, Hib meningitis incidence fell by 75% nationally (24 → 6 annual cases) and by 93% in the Grand Casa region (15 → 1 per 100,000 children under five) [5].
- ***Meningitis surveillance (2015-2018):*** Among 183 confirmed bacterial meningitis cases, Hib accounted for only 6%, primarily in unvaccinated children under five and adults [3].
- ***Diagnostic improvement (2018):*** RT-PCR applied to CSF samples detected Hi in culture-negative meningitis cases, demonstrating superior sensitivity and supporting the integration of molecular methods into national surveillance [4].

Algeria, Morocco, and Tunisia - Respiratory Resistance Patterns

A multicentric study (2006-2007) analyzing 262 respiratory isolates across three countries found:

- 13.3% of isolates resistant to amoxicillin due to β-lactamase production.
- Two isolates resistant to amoxicillin-clavulanic acid.
- All isolates susceptible to cefotaxime, cefixime, and levofloxacin [8].

Egypt - Adult Pneumonia Burden

A prospective study in Assiut University Hospital (2013-2014) found Hi in 16% of adults with community-acquired pneumonia:

- 71% were NTHi,
- 24% Hib,
- 5% serotype f [12].

High β-lactam resistance rates were also reported, highlighting the importance of surveillance beyond pediatric populations.

Libya - Data Gaps

No published epidemiological or resistance studies from Libya were identified in indexed medical literature [11]. Political instability and lack of structured surveillance likely contribute to this data gap.

Regional Summary

Country	*Study Context*	*Key Findings*
Tunisia	Pre- and post-vaccine invasive isolates	Hib dominance pre-vaccine; now 79% NTHi; resistance to ampicillin up to 42% [2, 6, 7]
Morocco	Vaccine impact & diagnostics	Hib meningitis reduced by 75-93%; RT-PCR improved detection [3-5]
Algeria	Respiratory isolates	13.3% amoxicillin resistance; cephalosporins effective [8]
Egypt	Adult pneumonia	16% Hi isolates (71% NTHi); high β-lactam resistance [12]
Libya	N/A	No published data; urgent need for surveillance [11]

Discussion

Hib Vaccine Impact and Epidemiological Shifts

The introduction of Hib conjugate vaccines in North Africa has dramatically reduced invasive Hib disease, particularly in children under five. In Morocco, incidence declined by 75% nationally and up to 93% in high-incidence regions such as the Grand Casa region [5]. In Tunisia, the post-vaccine period (2013-2023) shows a substantial decline in Hib prevalence, with Hib accounting for only 17% of invasive cases, while non-typeable Hi (NTHi) predominates at 79% [2].

The reduction in Hib incidence validates the high effectiveness of conjugate vaccines, consistent with global reports showing vaccine-mediated herd immunity [1, 4]. Decreased nasopharyngeal carriage of Hib not only protects vaccinated children but also reduces transmission to unvaccinated populations, including adults [1]. However, the continued occurrence of Hib infections in unvaccinated children and adults in both Tunisia and Morocco suggests that gaps in vaccine coverage and possibly waning immunity remain [2, 3].

The Tunisian three-dose schedule (2, 3, 6 months) without a booster may leave a small window of susceptibility in the second year of life [2]. While the long-term effectiveness appears robust, monitoring for potential resurgence remains important.

Serotype Replacement and the Emergence of Non-typeable Hi

Post-vaccination epidemiology demonstrates a clear shift from Hib dominance to non-typeable *H. influenzae* (NTHi), a pattern observed globally [2, 5, 6]. In Tunisia, NTHi now represents the majority of invasive cases (79%), with serotype a emerging at 4% [2]. The Sabrine Mzilem et al. study (2022) in Tunis provided in-depth molecular characterization of invasive typeable and non-typeable isolates, highlighting:

- The predominance of NTHi in invasive infections following Hib vaccination.
- Occasional persistence of type b (Hib) and rare type a strains, demonstrating that serotype replacement is complex and ongoing.
- The role of molecular tools, particularly PCR and WGS, in identifying serotypes and detecting resistance genes in both typeable and non-typeable isolates [2].

NTHi is increasingly recognized as a cause of severe invasive disease, especially in infants, elderly patients, and immunocompromised populations [2, 12]. The emergence of serotype a, although less common, has raised concern because of its historical virulence in other regions and its potential to cause outbreaks if unchecked [2]. This highlights the importance of continued molecular surveillance to detect emerging serotypes and guide vaccine policy.

Antimicrobial Resistance: Insights from Tunisia and Sabrine Mzilem's Work

The evolution of antimicrobial resistance (AMR) in *H. influenzae* is a major concern in the post-vaccine era. Studies from Tunisia, including those led by Sabrine Mzilem, provide detailed insight:

- ***Ampicillin resistance*** increased from ~27% in the pre-vaccine era (1999-2002) to 42% in 2013-2023 [2, 6, 7].
- ***Amoxicillin-clavulanate resistance*** reached 20%, while resistance to third-generation cephalosporins, including cefotaxime, remains low (4%) [2].
- ***Mechanisms of resistance:***
    - β-lactamase production (bla_{TEM-1}) was identified in 14 Tunisian invasive isolates [2].
    - Non-enzymatic resistance due to PBP3 (ftsI) mutations was detected in multiple NTHi isolates [2].
    - Some strains exhibited dual mechanisms, i.e., β-lactamase production and PBP3 modification, complicating therapy [2, 6].

The Sabrine Mzilem study underscored the critical role of molecular diagnostics in detecting these complex resistance mechanisms. Conventional phenotypic methods may underestimate resistance prevalence or fail to identify emerging variants, especially in non-typeable isolates [2]. Her work highlights the importance of ongoing molecular surveillance, not only to track AMR evolution but also to monitor the changing distribution of circulating serotypes over time.

These findings have clinical implications: ampicillin and other penicillins may no longer be reliable first-line agents for invasive *H. influenzae* in Tunisia. Third-generation cephalosporins, particularly cefotaxime, remain largely effective but vigilance is required given the emergence of rare resistant isolates [2, 7, 8].

Comparative Regional Perspective

Comparing North African countries illuminates differences in epidemiology, resistance patterns, and surveillance quality:

- ***Morocco***: Hib vaccination achieved remarkable reductions in disease incidence, and molecular diagnostics (RT-PCR) improved sensitivity in culture-negative meningitis cases [4, 5].
- ***Tunisia***: Sabrine Mzilem's studies reveal high NTHi prevalence, significant ampicillin resistance, and complex dual resistance mechanisms [2].
- ***Algeria***: Respiratory isolates (2006-2007) exhibited 13.3% β-lactamase-mediated amoxicillin resistance, but cephalosporins remained effective [8].
- ***Egypt***: Adult pneumonia studies show 16% Hi prevalence, 71% NTHi, and high β-lactam resistance [12].
- ***Libya***: Published data are scarce; surveillance gaps highlight the need for laboratory infrastructure and molecular diagnostics [11].

These differences underscore the need for country-specific interventions, even as regional trends such as serotype replacement and rising resistance are consistent. The Tunisian data, particularly from Sabrine Mzilem, serve as a benchmark for understanding how molecular surveillance can inform public health strategies.

Surveillance and Diagnostic Advances

The importance of molecular surveillance cannot be overstated. In Tunisia, Sabrine Mzilem's work used PCR and WGS to:

- Identify resistance genes (*bla*_{TEM-1}, *ftsI* mutations).
- Distinguish typeable from non-typeable strains.
- Track serotype replacement and emergence of rare serotypes.

In Morocco, RT-PCR on CSF samples improved detection sensitivity, especially in previously treated patients with culture-negative meningitis [4]. These advances enable timely identification of emerging threats, inform empirical therapy, and guide vaccination strategy adjustments.

However, challenges remain: surveillance coverage is uneven, particularly in Libya and rural areas of Tunisia, and adult populations are underrepresented in most studies [11, 12]. Building molecular diagnostic capacity and harmonizing data collection across the region are critical next steps.

Implications for Policy, Treatment, and Future Research

The findings of North African studies carry several important implications:

1. ***Vaccination Policy***: Maintain high coverage of Hib vaccines and consider booster doses or next-generation vaccines targeting NTHi and emerging non-b serotypes [2, 5].
2. ***Antimicrobial Stewardship***: Rising ampicillin resistance and dual-mechanism strains require rational use of antibiotics and updated clinical guidelines [2, 6].
3. ***Molecular Surveillance Expansion***: PCR and WGS should be integrated into routine surveillance to monitor resistance and serotype evolution [2, 4].
4. ***Regional Collaboration***: Shared surveillance networks can harmonize data collection, track cross-border spread, and coordinate public health responses [2, 5].
5. ***Research Priorities***: Studies on vaccine development against NTHi, serotype a, and other emerging strains, as well as investigation of AMR mechanisms, are urgently needed [2, 5, 12].

Knowledge Gaps

Despite progress, gaps remain:

- Post-2011 longitudinal epidemiological data in Tunisia remain limited, complicating assessment of long-term vaccine impact [2].
- Libya lacks published surveillance data entirely [11].
- Adult populations and community-acquired infections are underrepresented, though evidence suggests NTHi is increasingly important in adults [12].
- The clinical impact of emerging dual-resistant strains requires further study to guide empirical therapy.

Conclusion

Over the past two decades, Hib vaccination in North Africa has achieved remarkable success, dramatically reducing the burden of invasive Hib disease in children under five [2, 5]. Concurrently, the epidemiological landscape has shifted toward non-typeable strains and, to a lesser extent, other encapsulated serotypes such as serotype a. Antimicrobial resistance has emerged as a significant concern, with increasing prevalence of ampicillin-resistant strains mediated by β-lactamase production and PBP3 mutations [2, 6, 7].

Sustained vaccination programs, molecular surveillance, and antimicrobial stewardship are essential to maintain these public health gains. Moreover, the development of vaccines targeting NTHi may be necessary to address the rising burden of non-typeable infections. Finally, strengthening laboratory and surveillance capacity, particularly in countries like Libya and Egypt, is critical to ensure comprehensive regional control of *Haemophilus influenzae*.

The North African experience underscores the dual lessons of success and ongoing challenge: while Hib vaccination has saved thousands of lives, evolving serotype dynamics and antimicrobial resistance demand continued vigilance and innovation in both vaccination and treatment strategies.

References

1. World Health Organization. “Global burden of Haemophilus influenzae type b disease”. WHO (2000).
2. Mzilem S and Boukhchina S. “Typeable Ampicillin-resistant Haemophilus influenzae Strains in Tunisian Children”. Medicine (Baltimore) 101.38 (2022): e30713.
3. Ikken Y., et al. “Epidemiology of bacterial meningitis in Morocco (2015-2018)”. Acta Microbiol Immunol Hung 67 (2020): 243-251.
4. Ikken Y., et al. “Real-time PCR detection of H. influenzae from culture-negative CSF samples in Morocco”. Acta Microbiol Immunol Hung 68 (2021): 107-112.
5. Moroccan Ministry of Health. “Hib vaccination impact report, 2007-2009”. Rabat, Morocco.
6. Mzilem S and Boukhchina S. “Resistance to several antibiotics in Haemophilus influenzae strains”. Acta Med Mediterranea 37.1 (2021): 421-424.
7. Pre-vaccine surveillance, Tunisia 1999-2002. National Institute of Public Health, Tunisia.
8. Benbachir M., et al. “Antimicrobial resistance of respiratory pathogens in North Africa, 2006-2007”. J Chemother 21 (2009): 56-60.
9. Peltola H. “Worldwide Haemophilus influenzae type b disease at the beginning of the 21st century: global analysis”. Clin Microbiol Rev 13 (2000): 302-317.
10. World Health Organization. “Expanded Programme on Immunization guidelines”. WHO (2012).
11. Libya Health Ministry Reports, unpublished data, 2000-2023.
12. El-Mokhtar MA., et al. “Community-acquired pneumonia caused by H. influenzae in adults, Egypt 2013-2014”. Sci-Afric J Sci Issues Res Essays 2 (2014): 456-461.