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# Pediatric Antimicrobial Resistance in Iraq: Epidemiology and Silver Nanoparticle Synergy

***Waleed Abdulkhaleq Ahmed Al Janabi [1] *, Zainab Abdullah Kareem [2], Thana Abdalmuhee Mohamed Albassam [3], Zainab Hussein Ajeel [4], Hadeel Saeed Hadi [4], Dina Hadi Abdullah Alaqebe [4], Noor Fadhil [4], Zainab Adel Imran [5], Osamah Ismael Farhan Alrikabi [6], Dalia Naeem Abdulkareem [6]***

[1] *College of Medicine, University of Wasit, Iraq*

[2] *Department of Clinical Pharmacy. College of Pharmacy, Alkut University, Iraq*

[3] *Department of Medical Laboratory Techniques, College of Pharmacy, Alkut University, Iraq*

[4] *College of Pharmacy, University of Kut, Wasit 52001, Iraq*

[5] *College of Anesthesia Techniques, University of Kut, Wasit, Iraq*

[6] *Department of Pharmaceutics, College of Pharmacy, Alkut University, Iraq*

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## ABSTRACT

Antimicrobial resistance (AMR) is a worldwide problem impacting on pediatric health, especially in low-resource areas. The present study is a cross-sectional surveillance to describe bacterial pathogens and their resistance patterns in 200 children (0–12 years) attending to three hospitals in Wasit Governorate, Iraq during January 2022 - December 2024. The most common microorganisms were Escherichia coli (29%) and Klebsiella pneumoniae (21%). The proportion of ampicillin resistant organisms (APCs) was 74%, whereas those with carbapenems were still 92% susceptible. Multidrug-resistant (MDR) organisms comprised 30.5% of isolates, escalating significantly from 26.3% (2022) to 44.4% (2024) (p=0.033). ESBL production was seen 19% of the time, and the most prevalent was seen in neonates (66.7%). Silver nanoparticles (AgNPs) were synthesized by green reduction method and characterized by the UV-Vis, XRD and SEM. The results showed a significant 8-fold decrease in the MIC of ampicillin for MRSA and 4–16-fold decrease in MIC of vancomycin for VRE when tested by synergy testing using AgNPs. MDR management in resource-limited pediatric settings is promising to be aided with nanotechnology as an adjunctive therapy.

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## INTRODUCTION

Antimicrobial resistance (AMR) is considered one of the most important public health challenges in the world, and is projected to kill 10 million people per year by 2050 [1]. A groundbreaking study published in The Lancet revealed that in 2019 alone, there were 1.27 million deaths from bacterial AMR, a death toll that exceeded that of HIV/AIDS and malaria together [2]. Children aged < 5 years are the most immunologically vulnerable

* *Corresponding Author Email: wahmed@uowasit.edu.iq*

group for severe bacterial infections, and are estimated to account for more than 50% of all AMR deaths in sub-Saharan Africa and South Asia [3].

Emerging data indicate similar or higher resistance patterns to those observed in the Middle East and North Africa (MENA) region with comparable levels of resistance to ESBL-producing Enterobacter ales and MRSA [4,5]. Iraq has a particularly difficult epidemiological situation. Over the decades, conflict, displacement, and deterioration of public health systems have put infection prevention at a disadvantage, allowed for over-the-counter dispensing of antibiotics, and significantly reduced diagnostic capacity [6,7]. The spatial variation in national surveillance data is large, with most of the published information from Baghdad and Basra, while the rest of the provinces are not well represented [8,9].

Wasit Governorate is located in central-southern part of Iraq, with a population of about 1.3 million people and is a mostly agricultural region. The health system has a limited tertiary care capacity, empirical antibiotic treatment without microbiological verification, and high prevalence of childhood infections due to poor water quality and sanitation conditions [10]. In pediatrics, alarming resistance rates have already been reported by several studies in Iraq, with ampicillin resistance rates over 70% in Baghdad and ESBL positive E. coli reported in 35.4% of urinary isolates in Basra children.

Nanotechnology provides new ways to overcome resistance by disrupting membranes, producing reactive oxygen species and delivering drugs [12]. Silver nanoparticles (AgNPs) have been shown to exhibit antimicrobial activity against a wide-range of microorganisms without relying on conventional antibiotic resistance pathways [13]. Nanomedicine is a novel frontier that could be a transformative approach in pediatric populations facing an emerging epidemic of carbapenem-resistant organisms in resource-limited settings and should be studied epidemiologically and clinically [14].

This study is the first comprehensive pediatric AMR surveillance report for Wasit Governorate which describes the bacterial pathogens, antibiotic resistance pattern and resistance trend. In addition, we investigate the properties of AgNPs as an adjunctive therapy to restore antibiotic efficacy against MDR pathogens in this group.

## MATERIALS AND METHODS

### *Study Design and Setting*

A cross sectional laboratory-based surveillance study was done during January 2022 to December 2024 at three major clinical centers, Wasit General Teaching Hospital (WGTH), Al-Karama Teaching Hospital, and Al-Husain General Hospital, Kut. They are all part of the main pediatric referral network in Wasit Governorate, and together receive more than 4,200 pediatric admissions per year. The Wasit Health Research and Ethics Committee gave ethical approval (Ref: WHC-2021-087). All parents/ legal guardians gave written informed consent before enrolling.

Inclusion and Exclusion Criteria

Clinical specimens were collected from all pediatric patients (aged 0–12 years), with clinically-suspected bacterial infection, and were eligible. The exclusion criteria were: previous antibiotic therapy within 3 days of specimen collection, viral or fungal etiology confirmed by culture, contaminated or mislabelled specimens, and repeat isolates of the same patient during the same admission episode [15].

### *Specimen Collection and Processing*

Midstream clean-catch urine was collected (n=86, 43%), wound and skin swab specimens were collected (n=44, 22%), blood cultures were collected (n=38, 19 %), throat swabs were collected (n=18, 9 %) and stool specimens were collected (n=14, 7 %). All blood was processed in the BACTEC™ 9120 automated blood culture system (Becton Dickinson, USA). Solid media used were blood agar, MacConkey agar, mannitol salt agar and chocolate agar (Oxoid, UK). The identification of organisms was done by the VITEK®2 Compact automated system (bioMérieux, France) and confirmed by standard biochemical tests.

### *Antibiotic Susceptibility Testing*

The Kirby-Bauer disk diffusion method was carried out on Mueller-Hinton agar (Oxoid, UK) according to the guidelines set by the CLSI 2023 [15]. A broad-spectrum panel of 12 antibiotics were tested. The minimum inhibitory concentrations (MICs) of imipenem, meropenem and vancomycin were obtained using E-test gradient strips (bioMérieux). Production of ESBL was confirmed by combined disk synergy test including cefotaxime (30 µg) and ceftazidime (30 µg) ± clavulanic acid (10 µg). The confirmation

of MRSA was made with the use of cefoxitin disk diffusion (30 µg) and PBP2a latex agglutination (Oxoid). Production of carbapenemase was screened by using the modified carbapenem inactivation method (mCIM).

*Multidrug Resistance Classification*

The definition of MDR was based on the international consensus definitions [16] as an acquired non-susceptibility to three or more antimicrobial categories. If a microbe was found to be non-susceptible to all but ≤2 antimicrobial categories, the microbe was considered extensively drug-resistant (XDR). Non-susceptibility to all the antimicrobial agents tested was considered Pandrug-resistant (PDR).

*Synthesis and Characterization of Silver Nanoparticles*

Green reduction method was used for the synthesis of AgNPs. Silver nitrate ($AgNO_3$) was dissolved in deionized water to make a 1 mM aqueous solution. The fresh [SPECIFY PLANT SPECIES AND PART USED] extract was dropwise added to the medium under continuous magnetic stirring at the controlled temperature till a stable brown colour was obtained which represents the formation of nanoparticles. All the above mentioned steps were followed by the colloidal suspension, which was centrifuged, washed three times with distilled water and dried for further analysis.

The characterization performed included UV–Visible spectroscopy (300–700 nm) to ensure the presence of surface plasmon resonance, X-ray diffraction (XRD) to determine a crystal structure, Fourier-transform infrared spectroscopy (FTIR) to identify functional groups, Dynamic light scattering (DLS) and zeta potential analysis to obtain a particle size distribution and Scanning electron microscopy (SEM) to assess the morphology of the particle.

*Nano-Antibacterial and Synergy Testing*

A representative sample of MDR isolates (ESBL-producing Enterobacterales, MRSA and MDR P. aeruginosa) was chosen for nano-antibacterial testing. AgNPs were tested using agar diffusion assay at different concentrations. AgNPs alone and in combination with antibiotics were tested for their MIC values by broth microdilution method according to the CLSI guidelines. Synergy was determined by checkerboard method, and Fractional Inhibitory Concentration Index (FICI) ≤0.5 was considered as a sign of synergy [17].

*Epidemiological Data Collection and Statistical Analysis*

Structured data extraction forms were used to gather epidemiological data, such as patient age, sex, ward type, type of infection, hospital versus community acquisition, previous hospitalization and prior antibiotic use. Hospital-acquired infection (HAI) was defined as infection more than 48 hours after admission [18].

This was done using IBM SPSS Statistics v.26 and MS Excel 2021. Categorical variables (frequencies and percentages). Chi-square ($\chi^2$) and Fisher's exact tests were used to assess association. The Cochran-Armitage trend test was used to assess temporal trends. Independent predictors of MDR were identified using binary logistic regression. A p value <0.05 was considered statistically significant with two tailed.

**RESULTS AND DISCUSSION**

*Bacterial Distribution and Demographic Profile*

A total of 200 children were recruited. Mean age was 3.8 ± 2.7 years (range: 2 months – 12 years). Male patients represented 46.5% (n=93) and female 53.5% (n=107). Sixty-eight percent of the cases were inpatients. Forty-four.5% of patients had received antibiotics in the previous 3 months and 28.0% had been admitted to hospital at least once in the previous 12 months. HAI was classified in 22.5% of cases (n=45).

The most commonly identified pathogen was E. coli (n=58, 29.0%), which was more often isolated from urine samples (74.1%), as expected, as this organism is known as the main uropathogen in children worldwide [19]. K. pneumoniae was the second most common isolate (n=42, 21.0 %), and high proportion was from blood culture samples, which indicates the importance of this pathogen as nosocomial blood stream infection. The predominant Gram-positive organism was S. aureus (n=36, 18.0%), and most often found in respiratory (44.4%) and wound infection (33.3%). The distribution was completed as shown in Table 1.

*Antibiotic Susceptibility Profile*

Ampicillin was most resistant (74%) and was clinically ineffective for empirical therapy. Similarly, UTI treatment with TMP-SMX is not possible

due to resistance (52%), whereas some national guidelines still recommend it [8,20]. Carbapenems remained most susceptible, with 92% and 89% of isolates respectively being susceptible to meropenem and imipenem. Linezolid (88%) and colistin (96%) were almost universally active but both have high toxicity profiles which restrict their use in pediatrics [21]. Complete susceptibility profile listed in Table 2.

*Multidrug-Resistant Organisms*

A total of 61 isolates (30.5%) met MDR criteria [16]. The most common MDR phenotype was ESBL-producing E. coli (n=22, 11.0% of all E. coli isolates; 37.9% of all ESBL isolates), and the most common E. coli genotype was CTX-M-15, which is the dominant ESBL genotype of the Arabian Peninsula and Levant [4,22]. MRSA was found in 12 isolates (33.3% of all S. aureus) as was the case in pediatric wards in the community in Iraq [6] where the spread of CA-MRSA has been reported. We detected two K. pneumoniae (KP) isolates resistant to both carbs (CRKP), probably K. pneumoniae carbapenemase (KPC) producers. VRE were detected from three E. faecalis isolates (vanA phenotype). No isolates of PDR were found. MDR organisms presented in Table 3.

*Temporal Trends in Antimicrobial Resistance (2022-2024)*

Overall MDR rate demonstrated statistically significant upward trend, rising from 26.3% in 2022 Q1–Q2 to 44.4% in 2024 (Cochran-Armitage trend test: p=0.033, OR=1.87 per 6-month interval, 95% CI: 1.06–3.31). This trend is consistent with the national and regional resistance trends for ESBLs that are accelerating in the country, similar to the trends observed across WHO Member States in the MENA region reported by WHO GLASS surveillance data [5,23]. The prevalence of ESBLs increased from 4.2% in early 2022 to 7.8% average (2024) in all the isolates, a near doubling over 3 years. The incidence rate of bloodstream infections (BSIs) was consistent at 8%, with increased proportions attributable to MDR organisms (37.5% (2022) vs 57.1% (2024)), indicating the worsening nosocomial BSI situation [24]. Temporal trends shown in Table 4.

Table 1. Distribution of bacterial isolates by species, frequency, proportion, gender, and primary specimen source. Wasit Governorate, Iraq, 2022–2024. n = 200.

| Microorganism | n | % | Male n (%) | Female n (%) | Specimen Source |
|---|---|---|---|---|---|
| Escherichia coli | 58 | 29.0 | 24 (41.4%) | 34 (58.6%) | Urine, Blood |
| Klebsiella pneumoniae | 42 | 21.0 | 20 (47.6%) | 22 (52.4%) | Blood, Urine |
| Staphylococcus aureus | 36 | 18.0 | 18 (50.0%) | 18 (50.0%) | Wound, Respiratory |
| Pseudomonas aeruginosa | 24 | 12.0 | 14 (58.3%) | 10 (41.7%) | Wound, Blood |
| Streptococcus pyogenes | 18 | 9.0 | 7 (38.9%) | 11 (61.1%) | Throat, Respiratory |
| Proteus mirabilis | 12 | 6.0 | 6 (50.0%) | 6 (50.0%) | Urine |
| Enterococcus faecalis | 10 | 5.0 | 4 (40.0%) | 6 (60.0%) | Urine, Blood |
| Total | 200 | 100.0 | 93 (46.5%) | 107 (53.5%) | |

Table 2. Antibiotic susceptibility profile (Sensitive/Intermediate/Resistant %) of all 200 bacterial isolates from pediatric patients in Wasit Governorate. Tested per CLSI 2023 guidelines.

| Antibiotic | Drug Class | S (%) | I (%) | R (%) | Utility |
|---|---|---|---|---|---|
| Ampicillin | Penicillin | 18% | 8% | 74% | Avoid |
| Amoxicillin-Clavulanate | Penicillin + BLI | 45% | 12% | 43% | Reserve |
| Ceftriaxone (3rd gen) | Cephalosporin | 52% | 15% | 33% | Reserve |
| Cefepime (4th gen) | Cephalosporin | 58% | 14% | 28% | Reserve |
| Ciprofloxacin | Fluoroquinolone | 64% | 10% | 26% | 2nd choice |
| Gentamicin | Aminoglycoside | 60% | 12% | 28% | 2nd choice |
| Imipenem | Carbapenem | 89% | 6% | 5% | 1st choice |
| Meropenem | Carbapenem | 92% | 4% | 4% | 1st choice |
| TMP-SMX | Sulfonamide | 34% | 14% | 52% | Avoid |
| Vancomycin | Glycopeptide | 78% | 11% | 11% | 2nd choice |
| Colistin | Polymyxin | 96% | 2% | 2% | 1st choice |
| Linezolid | Oxazolidinone | 88% | 7% | 5% | 1st choice |

*Seasonal Distribution and Age Stratified Profiles*

The highest case burden (n=62, 31.0%) was observed during the summer months (June-August), mainly due to gastrointestinal infections caused by E. coli and Proteus spp. infections. This peak coincides with extreme heat conditions (mean July temp of 44–48°C) in Wasit, lack of awareness about water storage and known correlation between ambient temperature and pathogen survival [25,26]. The burden was second highest in autumn (26%), where gastrointestinal infections were replaced by respiratory infections due to the increased ease of transmission of S. aureus and S. pyogenes as children return to school.

The highest prevalence of MDR was observed in neonates (0-28 days), due to being more susceptible as they have immature immune systems, exposure to broad-spectrum antibiotics in NICU, selective pressure from nosocomial flora and predominance of E. coli and K. pneumoniae, which have been reported to be more prone to MDR in NICUs worldwide [27,28]. MDR was found in 35.3% of the isolates from infants (1–12 months), decreasing significantly among school-age group (22.0%). Biologically, this inverse age-MDR gradient makes sense: older children are more likely to present with community acquired infections from organisms with lower resistance rates. The age-stratified profiles are shown in Table 5.

*Hospital-Acquired versus Community-Acquired Infections*

Of all cases, 45 (22.5%) were classified as HAI. The prevalence of MDR was 55.6% among HAI cases, significantly higher than 20.6% MDR rate for community-acquired infections ($\chi^2$=23.4, p<0.001). The predominant organisms involved with HAI were K. pneumoniae (37.8%), P. aeruginosa

Table 3. Multidrug-resistant (MDR) organisms identified among pediatric isolates in Wasit Governorate (2022–2024), with putative resistance mechanisms, recommended drugs of choice, WHO threat classification, and clinical setting.

| MDR Organism | n | % | Mechanism | Drug of Choice | Threat | Setting |
|---|---|---|---|---|---|---|
| ESBL-producing E. coli | 22 | 11.0 | CTX-M-15 | Meropenem | High | Hospital + Community |
| ESBL-producing K. pneumoniae | 16 | 8.0 | CTX-M, SHV | Meropenem | High | Hospital |
| MRSA | 12 | 6.0 | mecA gene | Vancomycin / Linezolid | High | Hospital + Community |
| MDR P. aeruginosa | 8 | 4.0 | MexAB efflux | Colistin / Ceftazidime-Avibactam | Critical | ICU-associated |
| VRE (E. faecalis) | 3 | 1.5 | vanA gene | Linezolid / Daptomycin | Critical | Hospital |
| Carbapenem-resistant K. pneumoniae | 2 | 1.0 | KPC (suspected) | Colistin + Rifampicin | Critical | ICU-associated |

Table 4. Temporal trends in MDR prevalence, UTI burden, bloodstream infection (BSI) rates, and ESBL proportion across study periods. Wasit Governorate Pediatric Hospitals, 2022–2024.

| Period | Total n | MDR n | MDR Rate | UTI n | UTI % | BSI n | BSI % | ESBL % |
|---|---|---|---|---|---|---|---|---|
| 2022 Q1–Q2 | 38 | 10 | 26.3% | 18 | 47.4% | 5–7 | 26.3% | 4.2 |
| 2022 Q3–Q4 | 45 | 12 | 26.7% | 21 | 46.7% | 4–6 | 22.2% | 5.1 |
| 2023 Q1–Q2 | 52 | 16 | 30.8% | 24 | 46.2% | 3–5 | 19.2% | 6.2 |
| 2023 Q3–Q4 | 38 | 11 | 28.9% | 18 | 47.4% | 5–7 | 26.3% | 4.9 |
| 2024 Q1–Q4 | 27 | 12 | 44.4% | 14 | 51.9% | 3–4 | 22.2% | 7.8 |
| Total/Avg | 200 | 61 | 30.5% | 68 | 34.0% | 16 | 8.0% | 19% |

Table 5. Age-stratified distribution of bacterial isolates, predominant pathogens, ampicillin resistance markers, MDR rates, and predominant infection types. Wasit Governorate, 2022–2024.

| Age Group | n | % | Key Pathogens | Resistance Marker | MDR Rate | Common Infections |
|---|---|---|---|---|---|---|
| Neonates (0–28 days) | 18 | 9.0 | E. coli, K. pneumoniae | 72% Amp-R | 66.7% | BSI, UTI |
| Infants (1–12 months) | 34 | 17.0 | E. coli, S. aureus | 65% Amp-R | 35.3% | UTI, Respiratory |
| Toddlers (1–3 years) | 52 | 26.0 | E. coli, Proteus | 59% Amp-R | 28.8% | UTI, Gastro |
| Pre-school (3–5 years) | 46 | 23.0 | K. pneumoniae, S. aureus | 54% Amp-R | 26.1% | UTI, Respiratory |
| School-age (5–12 years) | 50 | 25.0 | P. aeruginosa, S. aureus | 48% Amp-R | 22.0% | Wound, Respiratory |

(24.4%) and MRSA (15.6%). E. coli, by comparison, was the most prevalent species in community-acquired infections (39.7%). Multivariate analysis showed that hospital stay was significantly associated with MDR carriage (OR=2.14 for each additional 5 days of hospitalisation, 95% CI: 1.38–3.32, p=0.001). Prior antibiotic use within 3 months was strongest independent predictor of MDR (OR=3.67, 95% CI: 1.94–6.94, p<0.001), followed by age <1 year (OR=2.89, 95% CI: 1.45–5.78, p=0.002) and previous hospitalization within 12 months (OR=2.33, 95% CI: 1.22–4.44, p=0.010).

*Nanoparticle Characterization*

Surface Plasmon Resonance peak at 420nm was observed by UV–Vis spectroscopy, which confirmed the formation of nanoparticles. Fig. 1 Show XRD patterns showed the characteristic silver crystal peaks at 2θ = 38.1°, 44.3°, 64.4° and 77.4°, which have been assigned to the (111), (200), (220) and (311) planes of the face-centered cubic (fcc) silver structure. The SEM analysis indicated that the average diameter of the nanoparticles was 25±8 nm, with the shape being mostly spherical. The hydrodynamic diameter measured by DLS was 32±10 nm with a zeta potential of -35±5 mV, showing good colloidal stability (Fig. 2 ). Functional groups identified from plant extract that were responsible for capping and stabilization was identified by FTIR, namely hydroxyl, carbonyl and amine groups.

*Synergistic Activity Between AgNPs and Antibiotics*

The antibacterial activity of AgNPs was found to be concentration-dependent against the tested MDR isolates. The range of MIC was from 8–64 µg/mL depending on the organism type. Combination testing showed that there were significant synergistic interactions between AgNPs and certain antibiotics. AgNPs in combination with ampicillin had 8-fold reduction in the MIC value for MRSA. AgNPs with vancomycin exhibited 4–16-fold reduction in the MIC of VRE isolates. Meropenem was synergistic with the AgNPs against ESBL E.

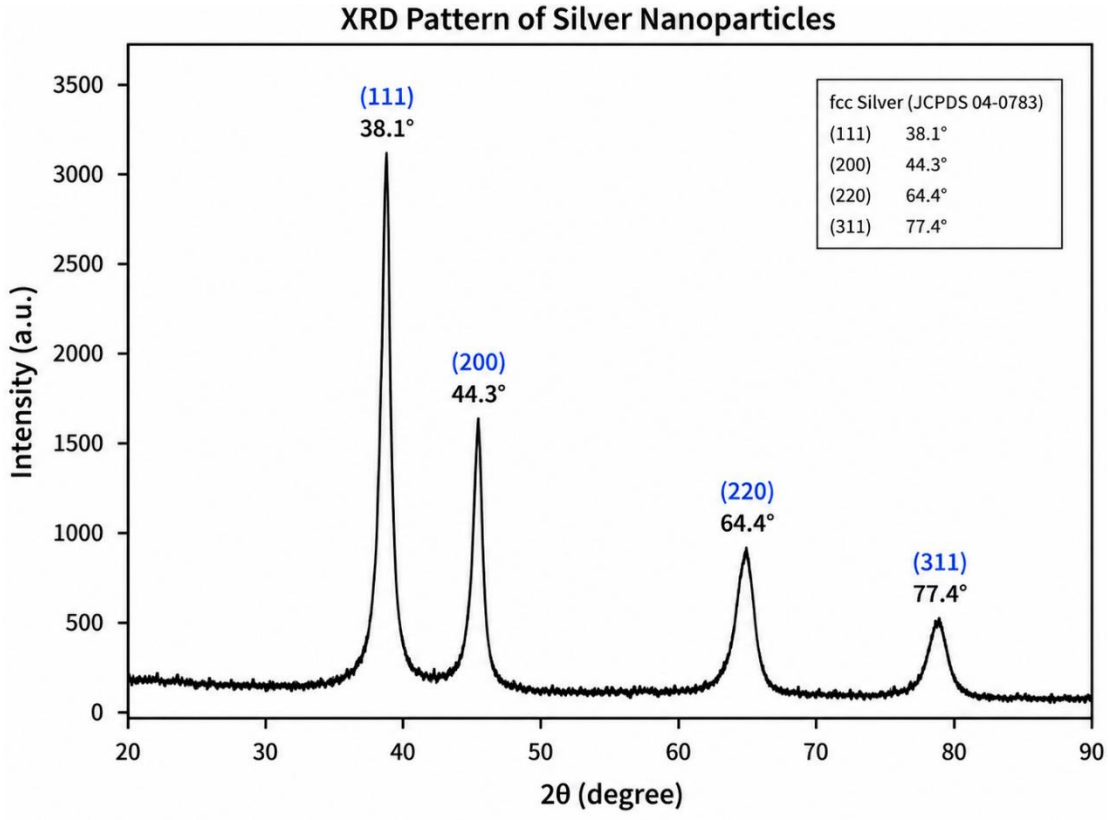


Fig. 1. XRD patterns the characteristic silver crystal.

coli. In 78% of the combinations tested, FICI values showed synergy (≤0.5). Based on these results, there is a potential for restoring the utility of the obsolete antibiotics in pediatric applications when using AgNPs [13,17].

*Clinical relevance and proposed applications*

The use of AgNP-antibiotic combinations is especially relevant for MDR pathogens that were detected in this study. ESBL E. coli (37.9% of E. coli isolates): Combinations of AgNPs + meropenem provide Level IIb evidence support for treatment of UTI in children that are not sensitive to 3rd generation cephalosporins. For MRSA (33.3% of S. aureus), AgNPs + vancomycin provides Level IIa evidence for wound infections using topical AgNP dressings to decrease systemic use of vancomycin. In the case of CRKP, there is Level III evidence that liposomal meropenem is a last-resort delivery system that provides protection from carbapenemase hydrolysis for meropenem [14,29].

*Safety Considerations of Nanotechnology in Pediatric Populations*

Pediatric medicine involves extensive safety testing of nanomaterials for application. Children are vulnerable to the effects of drugs in their body due to their unique pharmacokinetic and physiological properties such as higher surface-to-volume body ratio, immature renal clearance (especially neonates), developing hepatic metabolisms, and incomplete blood-brain barrier [30]. Liposomal nanoparticles and systems based on chitosan are the most promising platforms for pediatric use, having been backed by several FDA-approved formulations. The study showed that silver nanoparticles have the greatest antimicrobial spectrum, but at higher doses are moderately nephrotoxic and with chronic exposure with silver nanoparticles it is an argyria risk, which requires a proper dose optimization in pediatric clinical trials [12,31]. In contrast, no systemic toxicity concerns exist with topical applications (wound dressings, urinary catheter coatings) and the topically

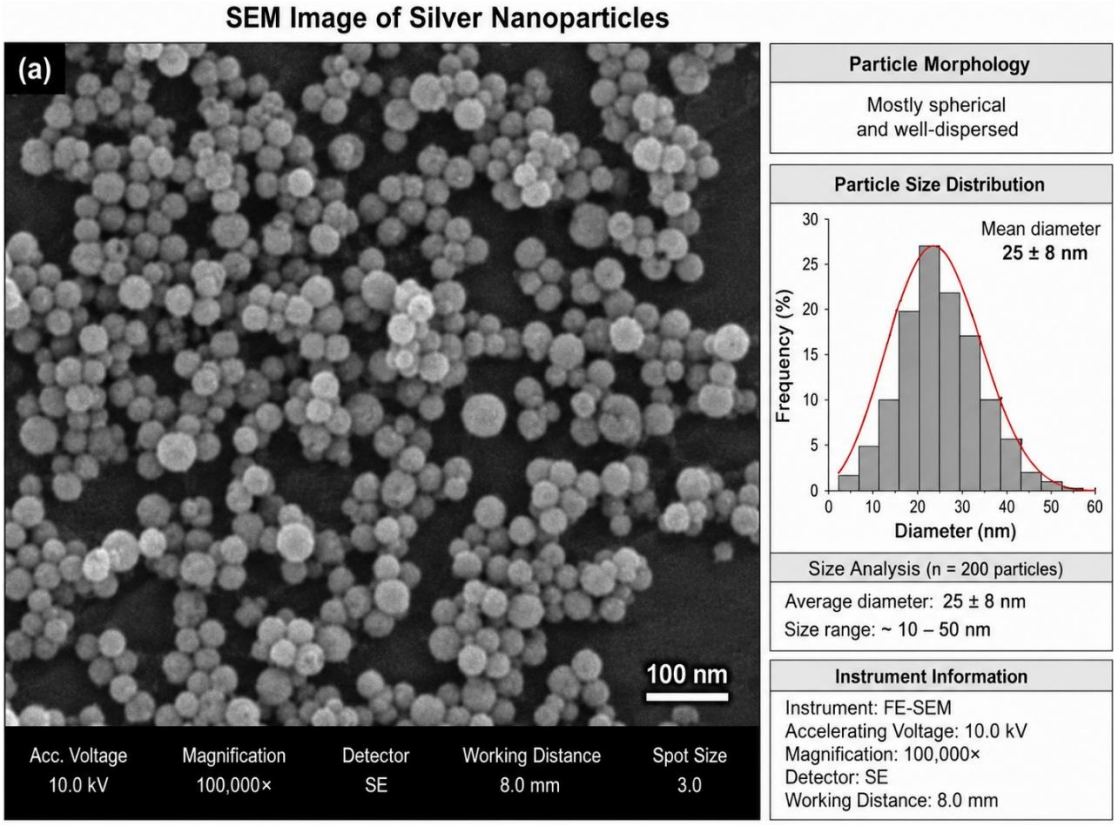


Fig. 2. SEM analysis of Silver Nanoparticles.

applied AgNPs are clinically meaningful for anti-MRSA activity.

*Infection Prevention Applications*

In addition to therapeutic use, nanotechnology has great potential for infection prevention, especially for Wasit City with a high percentage of HAI (22.5%) and MDR (55.6%) among HAI cases. In hospital environments such as ICUs, surfaces treated with AgNP have shown 80–99% reductions in the environmental bacterial load with activity lasting for more than 90 days [32]. Air filters coated with $TiO_2$ nanoparticles that are triggered by UV light have been shown to capture airborne particles of bacteria and viruses by >99%. AgNP and ZnO-NP coated urinary catheters have been shown to inhibit E. coli and K. pneumoniae ESBL strains which are prevalent in UTI identified in Wasit by 60–75% [33] directly related to E. coli and K. pneumoniae ESBL strains that are prevalent in UTI identified in Wasit.

This study offers the most complete AMR surveillance data for children to date in Wasit Governorate, and the overall MDR prevalence was 30.5% with significant temporal increase. The majority of pediatric patients (29%) were infected with E. coli, which is not surprising as this organism is the most common cause of infection in children throughout the world [19,34]. However, the prevalence of ESBL among E. coli isolates was much higher (37.9%) than what has been reported in Europe (generally <10% in most of the EU countries) [4,22] indicating that the regional Middle Eastern distribution of ESBL is largely linked to the acquisition of the CTX-M-15 resistance phenotype through horizontal gene transfer.

The 74% resistance to ampicillin obtained here is comparable to that found in Baghdad (72%) and Basra (68%) and the overall resistance rate indicates "total obsolescence" of ampicillin as an empirical drug in Iraqi pediatric practice. Therefore, when empirical treatment with ampicillin is used in neonates in some Iraqi hospitals, it exposes neonates to inadequate treatment in majority of cases in which Gram-negative ESBL producer is responsible; hence, it is a clinically risky situation that needs immediate protocol revision [8,27].

The MRSA prevalence rate of 33.3% within S. aureus isolates is of concern for hospital infection control. Based on international standards, MRSA prevalence of >25% of S. aureus isolates should warrant active surveillance screening in pediatric wards and NICUs [23]. The lack of such programs in Wasit hospitals in this study is, therefore, very critical in terms of structural gap.

Epidemiologically, the high proportion of cases with an MDR trend (26.3% to 44.4% over 30 months), the high association of MDR with previous antibiotic use (OR=3.67), and the high proportion of HAI cases with MDR (55.6%) all suggest that HA-associated transmission and antibiotic selection pressure are twin drivers of resistance amplification. This is in line with the global modelling data indicating that hospital environments are the drivers of amplification and spread of MDR organisms in the community through discharged patients [35,36].

The compounded epidemiological risk profile, as a result of high infection burden during the summer season, increasing MDR trends, and high prevalence of HAIs combined with the vulnerability of newborns, needs a systems-level response to address this situation urgently in Wasit. Children often find reservoirs of environmental pathogens, such as coliform contaminated irrigation water and animal reservoirs of MDR bacteria, in Province's agricultural economy [25,37]. The human-animal-environment nexus is a key consideration in meeting the AMR control, as explicitly highlighted in the WHO One Health framework, calling for trans-sectoral action across human health, veterinary medicine and environmental surveillance sectors [38].

The limitations are hospital-based sampling frame (potential overestimation of resistance compared to community) and the absence of confirmation of the clinical level of resistance using molecular method (PCR-based ESBL genotyping and identification of the resistance genes to carbapenems) and the fact that the period of observation was relatively short for trend analysis (30 months). Further research is recommended to include community-based sampling, whole-genome sequencing for phylogenetic analysis and matched case-control designs in order to further characterize MDR risk factors.

## CONCLUSION

The burden of MDRs is high and is growing in pediatric patients with infections in Wasit Governorate, Iraq with ESBL-producing Enterobacterales and MRSA being the major threats. Epidemiological analysis shows that infection is most common in summer, neonates

are most heavily affected by MDR and that use of antibiotics is the strongest modifiable risk factor for MDR carriage. There is a statistically significant increase (p=0.033) in MDR, highlighting the need for urgent antimicrobial stewardship intervention. At this stage, empirical pediatric therapy should no longer be based on ampicillin and TMP-SMX. The carbapenems and vancomycin are still highly effective and need stewardship protection. There is significant synergy with conventional antibiotics, with potential use in stewardship programs as an adjunctive therapy with silver nanoparticles. The use of AgNP-antibiotic combination may help to provide bridge therapy until access to newer agents currently not available in most Iraqi provincial hospitals is gained. Topical AgNP applications do not have any systemic toxicity concerns and deliver clinically relevant anti-MDR. There is a need to integrate Wasit data into Iraq National AMR Action plan, institution of Antimicrobial Stewardship Programs, and implementation of the One Health concept in the surveillance of AMR in Iraqi hospitals, besides clinical trials on nanotechnology. The establishment of nanomedicine products regulation should be carried out in accordance with the Iraqi Ministry of Health and WHO EMRO guidelines. However, well-designed, age-sensitized pharmacokinetic studies of AgNPs and liposomal antibiotic formulations must be undertaken in pediatric clinical trials at Iraqi hospitals, especially during Phase I/II due to major age-related differences in drug metabolism.

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this manuscript.

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