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RESEARCH ARTICLES

RESEARCH ARTICLE

A Novel Hybrid Approach for Solving the Traveling Salesman Problem: Combining Local Search Techniques for Enhanced Performance

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Abstract

The Traveling Salesman Problem (TSP) is a classic combinatorial optimization problem. It involves finding the most efficient route that visits a set of cities exactly once and returns to the starting point. The development of an efficient solution to this problem is of great practical importance, particularly in the context of logistical and transportation applications. Some of the classic local search methods that have been adopted in the quest for better solutions include 2-Opt, 3-Opt, Slide, and Swap. These methods generate neighboring solutions in a systematic manner, eliminating

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suboptimal routes and thus improving the quality of the solutions. Among these, the 2-Opt method involves the elimination of crossed edges in the route. In contrast, the 3-Opt extends this concept to more complex changes, and while it may have the potential to generate superior solutions, it does so at a higher computational cost. The aim of this study is to provide a comprehensive investigation of the performance of the four methods: 2-Opt, 3-Opt, Slide, and Swap. Additionally, this paper proposes a hybrid method, HLSA, which incorporates all four methods in a systematic and balanced manner: 30% 2-Opt, 30% 3-Opt, 20% Slide, and 20% Swap. This approach is designed to yield more optimized results. The results demonstrate that the HLSA is significantly faster and more effective than traditional algorithms, as evidenced by rigorous experimentation and comparison. Furthermore, the solution to TSP has been shown to be both practical and efficient, making it a viable candidate for real-world implementation.

1. Introduction

The TSP has been one of the most famous combinatorial optimization problems that has attracted the interest of the scientific community over the last few decades. The ultimate task of the problem is to find the minimum route that a salesman should travel in order to pass through several previously determined cities and then return once again to the current city. Moreover, each city can be visited only once, further increasing the difficulty of this problem. Because of the rapid growth in the number of possible combinations that a solution can take due to an increase in the number of cities, TSP, being a computationally intensive problem, makes the determination of an optimal solution cumbersome [1].

Exact algorithms and heuristics have tackled the TSP. Exact algorithms can provide only the optimal solution for small-size problems, while for large problem sizes, they become impracticable. Therefore, heuristic methods have become highly important in practice to quickly find good approximate solutions [2].

Some of the most used techniques for solving TSP include local search algorithms. In such algorithms, an initial solution is first obtained, which is then iteratively improved. The underlying idea is to get closer to a better solution by checking the neighbors of the solution in hand. This usually aims at the minimization of the total travel distance by changing the order or location of cities [3].

Combinatorial optimization problems are elementary mathematical building blocks that result in complexity and optimization concerns in many real-world areas of application [4]. Within these, one could mention TSP. The TSP is a problem wherein a salesman seeks to carry out a tour so that he is able to visit a certain number of cities at the shortest distance possible. Several heuristic methods and optimization algorithms have been developed within the literature for finding the solutions of such problems. This paper will discuss some key local search optimization techniques: 2-Opt, 3-Opt, Slide, and Swap.

2-Opt aims to better the TSP solution by exchanging positions in two cities in pursuit of a better route. The underlying basic principle of this method is to minimize the total distance traveled by changing the intersection point of two roads [1]. 3-Opt is an enhanced version providing a number of opportunities to look for the optimal path due to three different breakpoints within the tour [5]. This method requires much more problem calculations, yet it might lead to obtaining better results [3]. The Swap operator generates a new tour by exchanging positions of two cities [6]. The Slide operator attempts to produce a new tour by sliding one of the cities into a new position while keeping intact the order of the cities in the current solution [6].

Local search operators like Slide, Swap, 2-Opt, and 3-Opt have effectively dealt with the TSP. Nevertheless, these approaches may have limitations in certain situations. Hybrid approaches that combine various optimization tactics have proven to render better outcomes [7], [8], [9], [10], [11], [12]. For instance, 2-Opt and 3-Opt type local search methods can identify an exact tour alteration and provide near-optimal solutions. These local search methods can then be followed by Slide and Swap, which increase the area of search and enhance the results [6].

This paper proposes the Hybrid Local Search Algorithm (HLSA) algorithm, including different multi-local searches such as Slide, Swap, 2-Opt, and 3-Opt in solving TSP. This algorithm employs a dynamic weighting scheme, with the assignment of percentage weight to each local search method: 20% for Swap, 20% for Slide, 30% for 2-Opt, and 30% for 3-Opt, and then uses the roulette wheel for the selection of operators for every function call. In this methodology, the performance of the solution for TSP will be improved.

This paper consists of six chapters. Section 2 gives the overall review related to the TSP optimization and related concepts, identifying the key methodologies and approaches from earlier works. Section 3 describes the TSP problem in depth, entailing a description of the operators used, dataset selection, and details about the HLSA algorithm. Section 4 depicts the experimental results, considering HLSA against other optimization methods. Section 5 discusses the results in detail. Finally, Section 6 concludes the study by summarizing the essential findings and contributions of HLSA and highlighting the effectiveness of HLSA in delivering better solutions with lower computational costs. Furthermore, some of the possible avenues for future research are outlined, which may improve the algorithm's performance.

2. Related works

Deep learning and machine learning are widely used in solving various problems, such as optimization problems, data classification, object recognition, and natural language processing, among many others. These technologies have been applied in a wide range of applications, from post-pandemic education continuity [13] to hygiene monitoring systems [14] and waste management solutions [15]. Moreover, effective results have been achieved in complex tasks such as biological image classification [16], license plate recognition [17], transfer learning [18], and sign language recognition [19]. Successful results have also been obtained with AI-based models in medical tasks such as brain tumor classification [20].In particular, deep learning and AI-based methods have succeeded significantly in combinatorial optimization problems such as TSP. TSP is one of the basic problems of combinatorial optimization and is generally used to reach a solution to logistics, transportation, and planning problems. Within this context, in this section, we draw upon some critical works on TSP in the literature and introduce the different solution methods.

Khan and Maiti proposed an enhanced version of the ABC algorithm for tackling with TSP problems, exploiting some update rules along with K-opt operations [21]. All eight different update rules proposed in this work are done in a way that these update rules may help the swap operation on the sequence of cities in order to improve the quality of the solution paths. Bees update the solution in the algorithm using a randomized rule selection process via the roulette wheel selection process. At the same time, some stagnant solutions undergo K-opt operations to further improve the best solution quality. The algorithm's performance was evaluated on TSPLIB benchmark datasets, demonstrating satisfactory accuracy and consistency when compared to existing methods for symmetric and asymmetric TSP problems.

Zhao et al. proposed a hybrid approach that encompasses concepts of the simulated annealing method and local search in solving the TSP [12]. A valid tour is considered to be one that visits each city exactly once and then returns to the original city. The algorithm was enhanced by the addition of a simulated annealing component as well as a localized search technique. The computational tests performed on datasets that had never undergone any preprocessing returned promising results, confirming the effectiveness of this hybrid method.

Tongur and Ülker enhanced the MBO algorithm by adding neighborhood operators to obtain more effective solutions for TSP and TSP and asymmetric TSP (ATSP) problems [22]. While the basic Migrating Birds Optimization (MBO) algorithm was shown to be quite effective for solving quadratic assignment types of problems, in other more complex problems such as TSP and ATSP, the performance remains far from optimal. The experiment showed that the neighborhood operators had a very significant impact, up to 36%, on improving the performance of the algorithm. Experimental results from TSPLIB datasets confirmed that the modified MBO algorithm successfully solved TSP problems when optimized with different neighborhood operators.

Voudouris et al. consider the TSP to be one of the most famous problems in the field of combinatorial optimization [23]. They investigate how the techniques of Guided Local Search (GLS) and Fast Local Search (FLS) can be applied to such a problem. GLS builds on local search heuristics and aims to enable these processes to explore large search spaces of combinatorial optimization problems efficiently and effectively. GLS can be combined with the neighborhood reduction scheme of FLS, significantly speeding up the algorithm's operations. Combining GLS and FLS with TSP local search heuristics of different efficiency and effectiveness is investigated to determine the dependence of GLS on the local search heuristics used. Furthermore, comparisons are made with some of the best TSP heuristic algorithms and general optimization techniques, showing the advantages of GLS over alternative heuristic approaches proposed for the problem.

Gouveia and Paias et al. consider TSP with spatial consistency constraints [24]. Spatial consistency constraints mean that the location of the next visit point constrains a visit point. These constraints can arise, for example, when a healthcare provider, while visiting a patient, also wants to visit other patients in the same region [24]. The paper presents an algorithm for solving TSP with spatial consistency constraints. The algorithm is based on the tabu search algorithm and uses a set of tabu rules to find a route that satisfies the spatial consistency constraints.

Günay-Sezer and Çakmak et al. proposed a method to optimize drone movements using a hybrid meta-heuristic solution [11]. This solution combines the capabilities of genetic algorithm (GA) and tabu search (TS) algorithms. GA generates and refines travel routes, while TS facilitates continuous exploration without getting stuck in local optima. The proposed hybrid meta-heuristic solution outperforms classical methods in terms of solution quality.

Mosayebi and Sodhi, as described in their article, studied the complexities of the business time traveling salesman problem (TSPJ), in which a preset amount of time should be allotted to each customer [25]. Unlike the classic TSP, TSPJ necessitates optimizing travel routes and time spent with each customer. The method suggested in the article resulted in better outcomes than traditional methods.

Shi and Zhang conducted research on various solution techniques for TSP using artificial neural networks (ANN) [26]. The authors objectively found that ANN has significant potential for solving TSP. Their proposed method demonstrated superiority over classical methods and effectively solved TSP using ANNs.

Voudouris and colleagues conducted a study on the effectiveness of GLS and FLS techniques for TSP[23]. Gouveia and Paias introduced a heuristic algorithm for TSP that includes spatial consistency constraints [24]. Günay-Sezer and Çakmak proposed a hybrid meta-heuristic solution method involving drones and reported superior outcomes [11]. Mosayebi and Sodhi solve the TSPJ problem with customer lead times and reach a more skilled solution than what was provided by classical techniques [25]. Shi and Zhang applied ANNs to solve the TSP problem and showed that this approach can often ascertain better solutions than those obtained by using traditional techniques [26]. Both these papers indicate that optimization methods can be applied to different applications which at its core involves TSP and its variants. In the end, the literature review concerning the Traveling Salesman Problem demonstrates that extensive research has led to the development of numerous algorithms and techniques for solving this significant optimization problem.

A wide range of methods in literature has been applied to solve TSP and related problems. Local search algorithms were found particularly useful for tackling TSP [27], while the hybridization of techniques has been used in finding better solutions to combinatorial problems [28].

Lancia and Dalpasso introduced one new cubic-time 3-Opt algorithm to solve TSP, which yields substantial improvements in finding an optimum against traditional techniques [29]. They designed one new algorithm that turns out to be faster and more efficient for TSP challenges and returned an effective performance about the optimization of TSP.

Schmidt and Irnich introduce novel neighborhoods and iterated local search (ILS) algorithms to handle the generalized traveling salesman problem (GTSP), which is an extension of TSP involving an associated cost function for each customer [30]. The authors' approach surpasses conventional ILS methods on multiple GTSP test problems.

Gao et al. suggest utilizing a Chaotic Differential Evolution algorithm for optimization problems [31]. By integrating a chaotic local search component into the classical differential evolution algorithm (DE), Chaotic DE

enhances the algorithm's capability to evade local optima and maintain the search process, resulting in an effective optimization tool that has yielded successful outcomes with these methods.

Aly and Guadagni et al. demonstrated how local search algorithms can optimize ANNs [32]. By eliminating the need for derivative calculations, these algorithms effectively reduce the complexity of ANNs. The authors proved the efficiency of local search algorithms in reducing ANN complexity.

Various methods and approaches have been proposed for the solution of TSP and related problems. In summary, Lancia and Dalpasso proposed a 3-Opt motion detection algorithm for TSP, which is cubic-time efficient and achieves expedited outcomes [29]. Schmidt and Irnich proposed a new ILS algorithm for GTSP, resulting in superior results [30]. Furthermore, Gao et al. had shown that chaotic local search-based differential evolution algorithms constitute an effective method to deal with optimization problems [31]. Aly and Guadagni applied ANN optimization using local search algorithms to bring out the effectiveness of the approach [32]. These research contributions provided new techniques for solving TSP and similar problems, further enriching the field.

There are many diverse practical areas of application of TSP and other combinatorial optimization problems. Their solution ensures a reduction in cost and provides more productivity in the business sector, which is a great advantage. However, the intricate nature of these problems renders the application of traditional methods an arduous and ineffective process. A review of the literature reveals that hybrid techniques can yield superior outcomes compared to traditional methods. Consequently, hybrid approaches have the potential to effectively address TSP and related problems, and their applicability can be extended to more complex problems in the future.

This paper proposes a hybrid local search algorithm that can be regarded as an incorporating approach of several local searches for the solution of TSP optimization problems. In HLSA, a dynamic weighting mechanism is applied to distribute certain percentages of every local search method. This mechanism enables the algorithm to track the adaptation of an instance in any problem and selects the most effective technique at each iteration. The roulette wheel method determines the local calling operator for each function call. The primary objective of this method is to enhance the solution efficiency of TSP and other related combinatorial optimization problems.

3. Materials and Methods

3.1. Travelling Salesman Problem

The Traveling Salesman Problem is one of the most traditional problems in combinatorial optimization, which falls under the main fields of computer science and operational research. It is a type of problem in which a salesman is tasked with visiting a given number of cities exactly once and returning to the starting city (or a given starting point) while minimizing the total distance traveled. If cities are represented by nodes and roads by lines, the problem corresponds to finding the minimum cost closed path on the graph [33]. As the number of nodes in the problem increases, the time spent solving the problem increases exponentially; the exponential increase of the solution time in TSP with an increasing number of nodes is shown in Table 1 [33].

Table 1. Evaluation of Hamiltonian Cycles.

Number of Nodes	Number of Cycles (n-1)!	Time
12	39.916.800	0.004 second
13	479.001.600	0.04 second
14	6.227.020.800	1 second
15	87.178.291.200	9 second
16	1.307.647.368.000	2 second
17	(17-1)!	35 second

18	(18-1)!	10 hours
19	(19-1)!	7,5 days
20	(20-1)!	140 days
21	(21-1)!	7,5 years
22	(22-1)!	160 years
23	(23-1)!	3.500 year
24	(24-1)!	2 million years

When Table 1 is analyzed, it is seen that the number of cycles increases rapidly with the number of nodes, and the time required to complete this process increases dramatically. The computation times become quite long, especially when increases beyond 15 nodes are considered. This shows that Hamiltonian loops and similar problems become more challenging to solve as the number of nodes increases. The mathematical formulation of a TSP is given below.

Constraints:

$$\sum_{j=1,j\neq i}^{n} x(i,j) = 1, i = 1,2,\dots,n \tag{1}$$

$$\sum_{i=1,i\neq j}^{n} x(i,j) = 1, j = 1,2,\dots,n \tag{2}$$

$$\sum_{i,j\in S}^{n} x(i,j) \leq |S| - 1, \forall S \subset \{1,2,\dots,n\} \tag{3}$$

$$x(i,j) = \begin{cases} 1, & \text{if going from point i to point j} \\ 0, & \text{if going from point i to point j} \end{cases} \tag{4}$$

Here, the distance between points i and j is denoted as d(i,j), while x(i,j) represents the distance from point i to point j. Equations 1 and 2 ensure that each point is visited only once. Equation 1 ensures that each point is exited only once, while equation 2 guarantees that each point is visited only once. Equation 3 serves as a sub-round elimination constraint, eliminating any sub-rounds that may occur. In Equation 4, a value of 1 for x(i,j) indicates that a trip has been made from point i to point j, while a value of 0 indicates that no trip has been made.

Objective Function:

$$\sum_{i=1}^{n} \sum_{j=1,j\neq i}^{n} x(i,j).d(i,j) \tag{5}$$

The objective function of the TSP, also presented in Equation 5, minimizes the tour length by finding the shortest possible route that visits each city exactly once and returns to the origin city.

3.2. Local search

Local search is a strategy for finding a better solution to an optimization problem by making small changes around an existing solution [34]. Slide, Swap, 2-Opt, and 3-Opt are standard methods to perform these modifications [35]. This section will provide an explanation of the Swap, Slide, 2-Opt, and 3-Opt techniques.

3.2.1. Swap operator

The swap operator is a technique to solve the TSP problem by randomly selecting two cities and swapping their positions within the tour sequence. This action modifies the sequence of visits. Repeatedly using this operator allows exploration of various shorter tour configurations [36]. By adopting this approach, conflicts at edges are resolved, leading to the identification of promising solutions and, ultimately, a decrease in tour length. Although not guaranteeing the optimal solution, the swap operator remains a valuable tool for efficiently enhancing existing solutions [36]. Figure 1 illustrates how the swap operator operates.
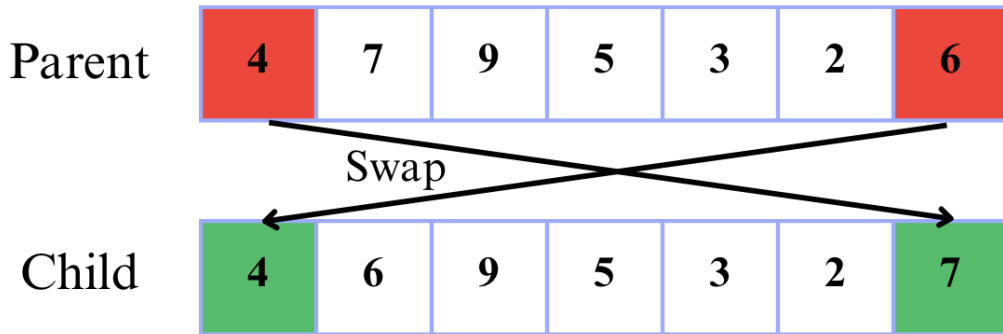
Fig. 1. The swap operator working principle.

3.2.2. Slide operator

The Slide is a fundamental operator used in TSP solutions. The Slide Operator moves a city to a new location without breaking the order of other cities. This maneuver explores shorter routes and prevents conflicts between edges to boost the tour's overall length [36]. The Slide Operator offers an alternative to the Swap Operator, allowing for examining new potential solutions by making slight changes to the arrangement of cities in the tour. This aids in enhancing the quality of the TSP solution by eliminating conflicts. However, like the Swap Operator, the Slide Operator does not ensure the best solution [37]. Figure 2 illustrates the working logic of the Slide Operator.
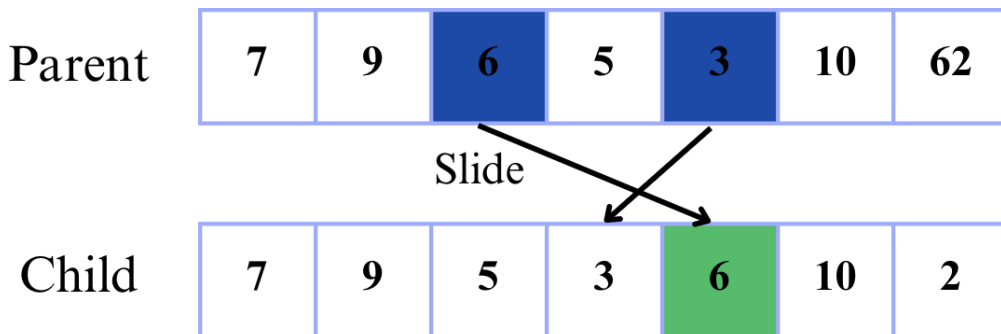
Fig. 2. The Slide operator working principle.

3.2.3. 2-Opt operator

The 2-Opt operator is utilized in TSP problem-solving methods to enhance solution quality by minimizing the total length of the corresponding tour. Unlike Swap or Slide operators, 2-Opt concentrates on eliminating diagonal edges present in the tour [38]. The 2-Opt operation identifies two such diagonal edges in the current TSP round. Once identified, these two edges are removed, which split the tour into two parts. The process of eliminating diagonals involves combining the two sections and reversing the order of city visits between the edges [39]. This procedure is repeated until no further improvements can be achieved. Although the 2-Opt technique is not infallible, it provides a systematic method to remove cross edges. The operational logic of this technique is depicted in Figure 3.
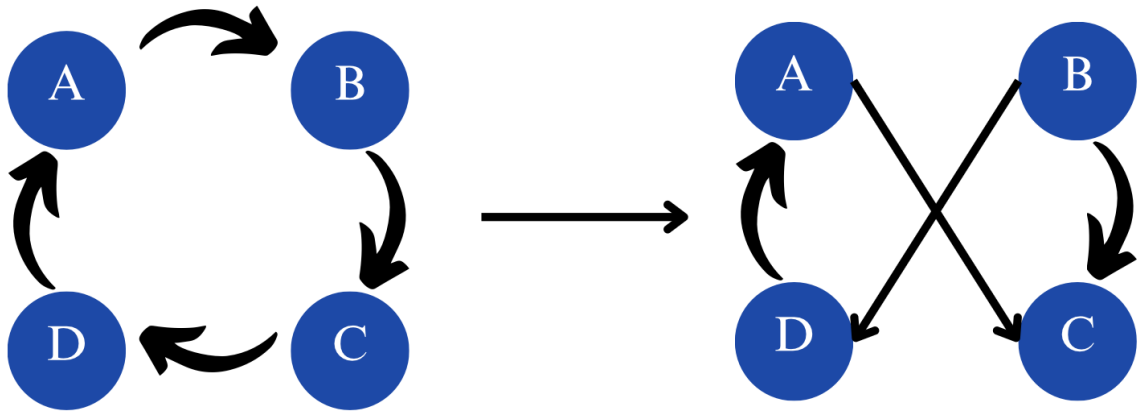
Fig. 3. The 2-Opt operator working principle.

3.2.4. 3-Opt operator

The 3-Opt operator is a method utilized for TSP problem-solving. The 3-Opt technique entails identifying three diagonal edges within the ongoing TSP round. By eradicating these three edges, the round is separated into multiple parts. The order of visiting the cities between these edges is reorganized to remove the diagonals, and the segments are then combined to create a novel tour. To explore various tour configurations, the same procedure is repeated multiple times [40]. It explores more tour possibilities than 2-Opt, but it does not guarantee the best solution of the TSP like other optimization processes. However, it is an essential tool used to improve the solution quality of TSP in the context of local search and optimization. Cheng et al. showed the working logic of the 3-Opt technique in their work [41].

3.3. Data set

The dataset for the study, which was retrieved from Traveling Salesman Problem Library (TSPLIB) [42], [43]. Introduction TSPLIB is a library of sample instances for the TSP (and related problems) from various sources and of varying size, which have been compiled over several years. TSPLIB instances have city coordinates, distance information between cities, and other necessary info to model TSP, which researchers employ for evaluating numerous algorithms/heuristics of TSP in comparison [42]. The data obtained from the TSPLIB library and the number of cities are presented in Table 2.

Table 2. Cities used in the study.

Dataset	Eil76	Berlin52	Rat99	St70	KroA100	Lin105	KroA200
# of regions	76	52	99	70	100	105	200

3.4. Proposed model

Various optimization operators are used to solve TSP problem [21]. The Slide operator moves one city without disturbing the order of the others and allows to find shorter routes. Swap tries to optimize the total route length by swapping two cities within the tour. 2-Opt reverses the order of cities when removing two diagonal edges in the tour, while 3-Opt does the same to remove three diagonal edges. These optimizations are used to improve SP's existing solutions quickly, but they do not guarantee finding the best solution. After testing all four methods, we created a hybrid method, HLSA, which combines all four methods (Slide, Swap, 2-Opt, 3-Opt). The distribution of 20% for Swap, 20% for Slide, 30% for 2-Opt, and 30% for 3-Opt was selected after a series of preliminary experiments. These proportions were determined based on the performance of each operator during these trials. The 2-Opt and 3-Opt operators, being more computationally intensive, were assigned higher weights as they consistently yielded superior results for larger datasets. On the other hand, the Swap and Slide operators, which execute faster but offer incremental improvements, were assigned equal yet lower proportions to maintain diversity in search space exploration. Such a balance enables the algorithm to explore global and local optima effectively, preventing it from incurring high computational costs. A more uniform distribution, such as 25% for each operator, was tested but yielded suboptimal results, as the algorithm could not fully leverage the strengths of the 2-Opt and 3-Opt techniques. The roulette wheel method determines the algorithm to choose, and what is its likeness. Roulette wheel method: This is a simple and effective probability selection algorithm that chooses from among many items or options [44], [45], [46]. This is used mostly in optimization problems. Its simple idea is to design a system where the chance of picking each option will be directly proportional to some quality or criteria amongst all options.

A random number between 0 and 1 is generated at the beginning of our algorithm. Based on the value of this number, the following selection process occurs:

- If the number is between 0 and 0.2, the Swap operator is selected.
- If the number is between 0.2 and 0.4, the Slide operator is selected.
- If the number is between 0.4 and 0.7, the 2-Opt operator is selected.
- If the number is between 0.7 and 1, the 3-Opt operator is selected.

Then, the distance is calculated and saved. Then, the next iteration is started, and the above operations are repeated. If the new solution is better than the one stored in memory, the new solution is saved; otherwise, the new solution is forgotten. This way, the process continues until the end state is reached and the shortest path is found. The structure of our HLSA model is given in Fig. 4.
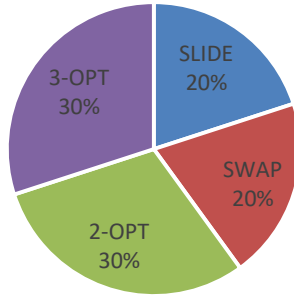
Fig. 4. Structure of the HLSA model.

To make the functioning of the HLSA algorithm clearer, the pseudo-code of the HLSA algorithm is given below.

pseudo-code of the HLSA algorithm

Initialize:
  - Define dataset from TSPLIB.
  - Set initial route and memory solution.
 	
While stopping criteria is not met:
  - Generate a random number between 0 and 1.
  - If $0 \leq$ random number < 0.2, apply Swap operator.
  - If $0.2 \leq$ random number < 0.4, apply Slide operator.
  - If $0.4 \leq$ random number < 0.7, apply 2-Opt operator.
  - If $0.7 \leq$ random number ≤ 1, apply 3-Opt operator.
  - Evaluate new route.
  - If new route is better than current memory solution, update memory.
 	
End While:
  - Return the best route found.

4. Results

This study combines the local search algorithm operators to solve the TSP, and the HLSA algorithm is created. The proposed HLSA model was run in MATLAB version R2023a on the Windows 11 operating system and a computer with Intel i5, 2.5 GHz processor, and 8 GB RAM. Table 3 shows the results of Slide, Swap, 2-Opt, 3-Opt and HLSA methods on eight different datasets. All algorithms were run under the same conditions and on the same datasets. The results in the table are measured in path length, which is the total length of the route determined by each algorithm. A lower path length means that the algorithm performs better and completes the trip in a shorter distance. The shortest paths (most successful results) are shown in bold.

Table 3. Local search optimization algorithms (Swap, Slide, 2-Opt, 3-Opt, and HLSA).

Data Set	Swap	Slide	2-Opt	3-Opt	HLSA
Eil76	690.65	652.65	600.52	590.45	**571.43**
Eil51	520.85	490.35	470.95	460.92	**449.96**
Berlin52	7920.65	7880.65	7850.96	7840.80	**7821.64**
Rat99	1450.55	1420.53	1398.12	1396.24	**1388.85**
St70	825.52	795.52	760.41	762.20	**743.92**
KroA100	24190.62	24160.52	24130.20	24140.20	**24129.07**
Lin105	16420.63	16400.63	16386.96	16381.20	**16380.93**
KroA200	32312.54	32302.24	32271.85	32270.40	**32253.39**

Table 3 presents the results of the Slide, Swap, 2-Opt, 3-Opt, and HLSA methods applied to eight different datasets. When analyzing these data, it is evident that the HLSA consistently produces the most successful results across all problems. Specifically, for datasets such as Eil76, Eil51, Berlin52, Rat99, St70, KroA100, Lin105, and KroA200, the HLSA generated shorter, more cost-effective paths than the standalone methods.

These findings demonstrate that the hybrid nature of HLSA combining multiple local search strategies provides a significant advantage over applying individual operators in isolation. For instance, while techniques like Swap or Slide might offer faster iterations, they tend to get stuck in local optima, which limits their effectiveness when dealing with more complex problem instances. On the other hand, although more computationally intensive, the 2-Opt and 3-Opt methods can explore a broader solution space, leading to better overall solutions.

Importantly, our assertion is not that HLSA will necessarily beat the standalone methods in speed. Certainly, operators like Swap or Slide can converge faster on their own because they are very simple. But the real power of HLSA is not in its speed but ratherin how good it can do and use that capability to produce high-quality solutions across diverse datasets. The hybrid algorithm is that it explores (through operators such as 2-Opt and 3-Opt) but exploits (Swap, Slide), subsequently producing better paths by preventing from becoming stuck into local optima. These findings are also corroborated by the consistently lower cost values provided by HLSA relative to other techniques.

Moreover, Fig. 5 illustrates the coordinates of the optimal paths identified by the HLSA algorithm across the eight datasets, underscoring the effectiveness and reliability of the approach. Moreover, the convergence behavior of the algorithm can be observed in the cost function plots in Fig. 6, which depict the function calls versus the cost for each dataset. These plots further demonstrate that while HLSA may require more iterations to converge in some cases, the solutions it produces are consistently superior to those obtained by standalone methods.

Ultimately, HLSA's effectiveness comes from its ability to combine the strengths of different operators, leveraging the global search capabilities of 2-Opt and 3-Opt alongside the faster but more localized improvements offered by Swap and Slide. This strategic combination enhances the search process, providing more optimal solutions for many TSP instances.
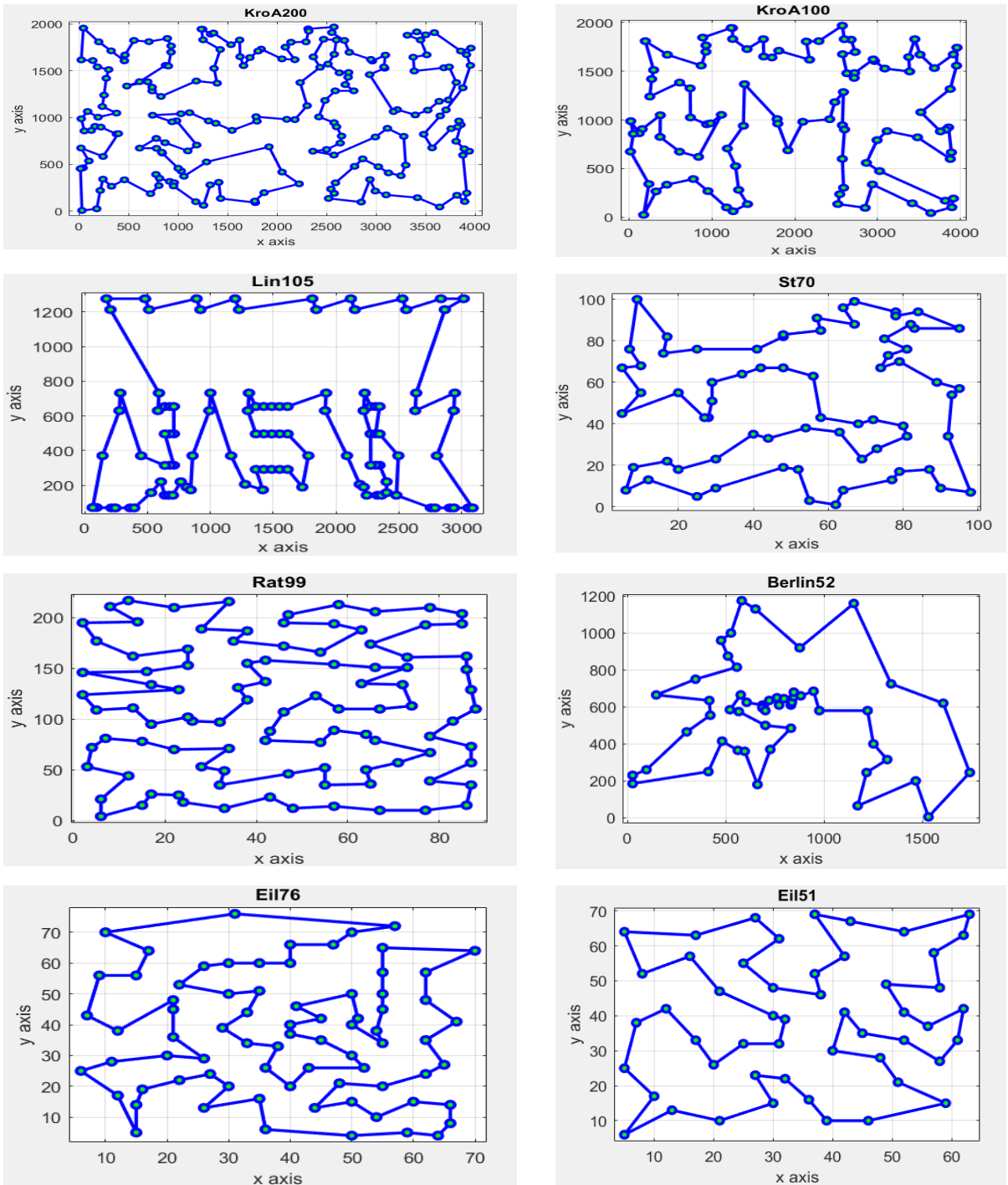
Fig. 5. The best coordinates found by HLSA.

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Fig. 5 shows the best paths found by the HLSA algorithm for eight different datasets (Eil76, Eil51, Berlin52, Rat99, St70, KroA100, Lin105 and KroA200). In each panel, we can see the placement of the cities in the dataset on the shortest path and how this path was optimized. It is possible to observe from these visualizations how the HLSA algorithm provides an effective solution on different dataset. Fig. 6 presents the Cost Function plots of HLSA for eight different datasets.
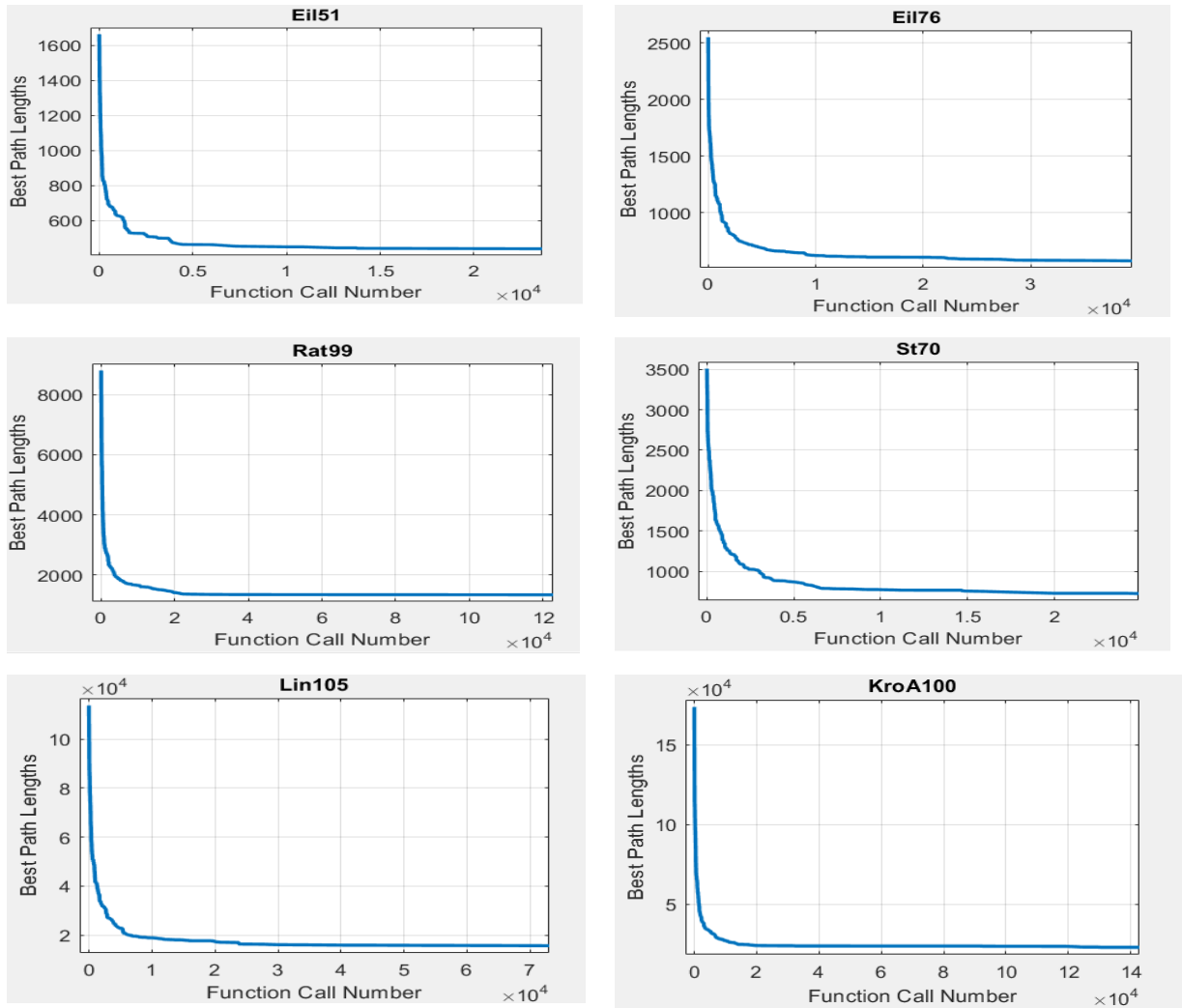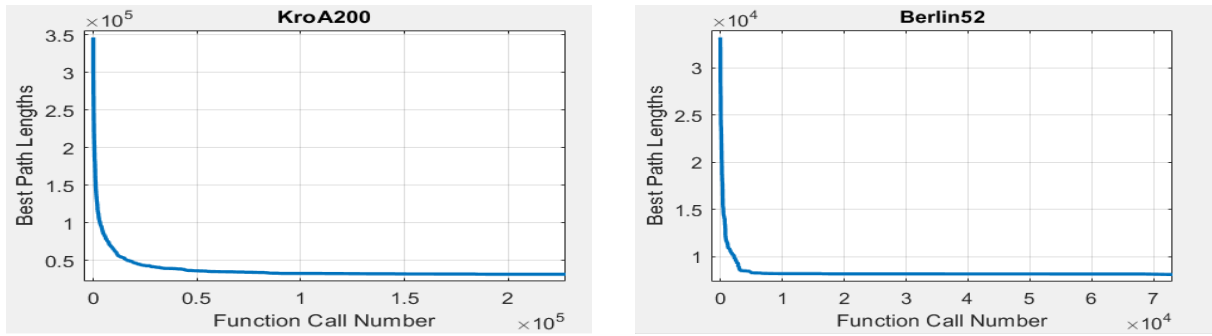
Fig. 6. Cost Function graphs of HLSA.

The performance of the HLSA algorithm was evaluated using eight TSP datasets. Analysis of the cost function graphs resulting from the algorithm operation reveals the following outcomes:

The algorithm identified the optimal solution for Eil51, Berlin52, and St70 datasets with 2000-7500 function calls. The algorithm demonstrated high performance for these datasets. For the Eil76 dataset, the algorithm determined the optimal solution with 10,000 function calls. The algorithm also performs well on this dataset. It achieved the optimal result with 20,000 to 50,000 function calls for the Rat99, Lin105, KroA100, and KroA200 datasets. However, the performance of these datasets is relatively inferior compared to the results obtained from other well-known optimization techniques such as Ant Colony Optimization (ACO), Genetic Algorithms (GA), and Artificial Bee Colony (ABC) [47], [48], [49], [50]. While these algorithms may outperform the proposed Hybrid Local Search Algorithm (HLSA) on specific large datasets, our method offers significant simplicity, computational efficiency, and hybrid adaptability advantages. By dynamically combining local search techniques (Swap, Slide, 2-Opt, and 3-Opt), HLSA balances exploration and exploitation, leading to more efficient problem-solving on medium-sized datasets with fewer computational resources. While other methods may offer better global solutions for highly complex problems, our approach is particularly suitable for real-world applications where computational time and simplicity are critical. Moreover, the hybrid nature of HLSA allows it to converge faster. It requires fewer parameters to be tuned compared to ACO, GA, or ABC, making it a more practical option in time-sensitive or resource-constrained environments.

The HLSA algorithm's performance varies with dataset size. It is concluded that as the number of cities or data points increases, the algorithm requires more computations, and the convergence process lengthens. Based on these findings, the HLSA algorithm proves highly efficient for the travel salesman problem. Nonetheless, the algorithm's performance dwindles as the size of the dataset increases.

5. Discussion

In this study, the HLSA aims to demonstrate the power of combining classical local search techniques by introducing a probabilistic structure for solving complex optimization problems, such as the TSP. The results indicate that HLSA offers more effective solutions than other methods across various datasets. However, specific key points should be emphasized to understand the findings better.

One of the primary advantages of HLSA is its ability to reduce the risk of being trapped in local optima through probabilistic operator selection. This enables the algorithm to explore a broader solution space, balancing local and global search capabilities. Particularly in larger datasets, such as KroA200, this probabilistic structure enhances the algorithm's capacity to find more effective solutions where other methods fall short. Such probabilistic approaches have been widely supported in the literature. Gu and Huang have demonstrated that combining various local search

techniques increases the chances of reaching the global optimum [27]. Similarly, Kaabachi et al. highlight the effectiveness of hybrid methods in solving combinatorial problems like the TSP [51].

In the literature, there are metaheuristic methods that outperform others in solving TSP, such as Simulated Annealing, Genetic Algorithms, and Tabu Search, which may yield shorter path lengths for specific datasets. However, these methods' complexity and long computation times, especially for large datasets, present a significant disadvantage. In contrast, HLSA combines simpler and faster local search techniques, such as Swap, Slide, 2-Opt, and 3-Opt, into a hybrid structure, resulting in lower computational costs and faster solutions. This makes it more applicable compared to complex methods, offering an effective alternative, particularly for small and medium-sized problems. A number of hybrid approaches have been proposed that make use of local search techniques and it has been demonstrated by researchers that these methods can produce good results even on large datasets [52], [53], [54].

The probabilistic nature of HLSA helps reduce the risk of getting stuck in local optima while combining global and local search capabilities. This flexibility allows the algorithm to explore broader solution spaces where other methods are confined to a single search strategy. In the literature, methods like GRASP (Greedy Randomized Adaptive Search Procedures) have demonstrated how such diversity can improve solution quality [55].

Metaheuristic algorithms often require very long execution times, especially for large data sets, and the computational cost may put a burden that we can hardly afford them. HLSA takes advantage of the simplicity that classical local search operators provide and in turn provides faster results with a lower cost. For example, Ant Colony and Genetic Algorithms achieve good results with large datasets but they are also known for heavy computational usage [47], [48]. The method of using a HLSA, in contrast, provides an approach that is more reasonable and still removes most of these costs.

The purpose of this work is to show that the combination with local search methods in a probabilistic hybrid framework leads to better results. Using the hybrid techniques can improve and come up with a solution that is of good quality at relatively lower computational cost. To sum up, by pooling the resources of classical local search methods in a hybrid manner HLSA serves as providing lower computational costs and more give head for solution strategies. The results from this study confirm that HLSA is a new way of solving the TSP problem. The use of hybrid search models is a competitive and strong option for optimization issues as TSP. Future research could involve further enhancements and optimization strategies to improve the performance of HLSA.

6. Conclusion

This This paper presents evidence supporting the efficacy of the proposed HLSA for solving the TSP. The hybrid approach, which combines four distinct local search methods (Swap, Slide, 2-Opt, and 3-Opt), yielded shorter paths and lower-cost outcomes in experiments conducted on disparate datasets. The efficacy of HLSA is evidenced by its superior performance compared to other methods, particularly for medium-sized problems. Furthermore, the test results on different datasets demonstrated that HLSA can explore a vast solution space and circumvent the local optima trap.

One of the most significant advantages of the algorithm is its ability to strike a balance between global and local search capabilities by combining different local search methods. The methodology uses the efficiency of more detailed and slower approaches, like 2-Opt and 3-Opt, with faster ones such as swap and slide, so this concept represents a hybrid structure. Notably, despite the increase in computational time for large datasets, the solution quality offered by HLSA is quite satisfactory in comparison to more costly and time-consuming algorithms. In conclusion, this research demonstrates the potential of hybrid approaches to combinatorial optimization problems and proves that HLSA offers an innovative solution to challenging problems such as TSP.

For future work, it is recommended that HLSA be combined with new optimization techniques to improve its performance, especially on larger datasets and more complex problems. Moreover, a more advanced adaptive structure, in which the weights of different local search methods are dynamically adjusted, can further improve the efficiency of the algorithm.

Author contribution

C.H.A., H.T., S.D, and D. Ö. actively participated in conducting the experimental studies and writing the manuscript

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RESEARCH ARTICLE

AR Book, augmented and mixed reality applications in the education of mineral processing machines

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Abstract

This study investigated the effects of three different augmented reality (AR) applications on the education of mineral comminution and classification machines. In the first application, an augmented reality booklet (AR-Book) was prepared, which included the basic machines used in mineral processing and classification. The application was designed for mobile devices and has an image target type structure. In the second application in the image target type, the mixed reality (MR) device MS Hololens 2 was used, which provides visualization in the environment and hand interactions on the models. The third application has a spatial-ground plane structure that provides hand interaction experience with MS Hololens 2. The contributions of these approaches, which aim to support traditional training, were examined through student feedback. As a result, student assessments, it was concluded that

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they improve learning, increase focus, make education more fun, and positively affect both the retention of knowledge and the overall quality of education.

Keywords: Mineral Processing; Augmented Reality; Mixed Reality; AR Book; Unity; Hololens 2

1. Introduction

Unlike virtual reality, augmented reality (AR) is a relatively new technology in which virtual designs can be intertwined with the environment without being isolated [1, 2, 3]. Although it dates to 1968, the major advancement in today's usage occurred with the ARToolKit software in 2000. The brief history of AR journey is explained with milestones in the Assemblr [4]. AR content includes visual, auditory, and haptic aspects [5]. Mobile devices and smart glasses are used as basic hardware. It is also possible to interact with these holographic images generated in living spaces, which are known as mixed reality (MR). In other words, MR is a composition of the physical environment and digital worlds through multiple sensors, advanced optics, and holographic processing [6].

It can be used in many areas, such as engineering, science and health sciences, education, work safety, geographic sciences, communication, etc. [7]. If it is considered specifically for education, the contribution of both virtual reality and augmented reality to classical education has been demonstrated by many scientific studies [8, 9, 10, 11].

There exist various virtual and augmented reality applications in mining engineering education [12, 13, 14]. Most of them use virtual reality, and some of them use partly augmented reality. The dominating scope of these studies is related to mining operations of open pits and underground galleries, tunnels and settlements [60-69]. On the other hand, there are a very limited number of studies [25-28] in which VR and AR are used in the training of mineral processing machines, and there are none for *augmented reality books, image and ground plane applications of mixed reality on mineral processing machine training*.

AR Books, as one of the branches of AR applications, represent a creative blend of traditional literature and digital media. They strive to offer an engaging reading experience by incorporating interactive features like 3D models, animations, audio, and videos, enabling readers to connect with the narrative in fresh and exciting ways [15].

The most up-to-date and advanced hardware in the AR field is smart glass. The most senior of these devices, products of high electro-optic technology, are Microsoft Hololens [16], and the newest is Apple Vision Pro [17].

Based on this strong infrastructure from the past to the present, an application was made in the field of mineral processing by using Unity's real-time development engine [18]. An AR Book was designed for the most basic machines, and first, a deployment was made for mobile devices that everyone can access. A second application was made using the Image Targets approach for the same AR Book, using MS Hololens 2 smart glass. With the application, hand interaction is also possible with the virtual machine models that appear on the AR Book. Drag, rotate, and scale operations can be performed with hand interaction, which is a realization of the concept of MR. The third application, a study called ground plane, was made for MS Hololens 2. Virtual models of machines appeared in space without the need for any Image Target. It is possible to intervene in these models with hand interaction and investigate them by handling or walking around them. This is also an MR application.

In augmented reality, packages and engines such as AR-Foundation, AR-Kit, and Vuforia. Vuforia [19] was preferred in this study due to its practical compatibility with Hololens 2 for mineral processing applications. Target shapes were loaded into the created database. Then, a *unitypackage* file was created and downloaded.

To measure the contribution of the study to education, which is the purpose of the study, students were asked for their opinions. In this way, the study is a novelty for mineral processing education in Turkiye.

Because augmented and mixed reality is a totally different approach in comparison to virtual reality, it has its own characteristics and study area. The scope of this study focused on *augmented reality and mixed reality* applications by using mobile devices and Hololens 2 for *mineral processing machinery and its training*.

2. Material and Method

In this study, Unity real-time development engine and Vuforia AR engine were used for the three applications to be aimed to develop. Two of the three applications in the study are called image targets, which are the camera reading the specially formatted and displaying three-dimensional models, animations and videos on them. The difference between them is in the deployment process to mobile devices or Hololens 2 devices and the subsequent hand interaction capability.

The third application, called the ground plane, displays models, animations, and videos on the ground or the surface scanned in space. Hand interactions are also offered in this application.

In the Unity project created, depending on the first scenario, JPG or PNG-type images of mineral processing machines were prepared to be used as image targets, and three-dimensional models with FBX, OBJ, or DAE extensions were prepared. 3D models were obtained from sharing sites such as GrabCAD [20], Warehouse Sketchup [21], Rigmodels [22], and Sketchfab [23]. A database with fifteen machines was created in Vuforia (Fig.1), and the package created here (unity package) was downloaded and imported to the Unity scene. As seen in the figure, a quality rating is expressed in stars for each figure added to the database. A quality of five or four stars is required to avoid mismatch and failure during viewing.

Hololens targeted applications also require the installation of Visual Studio (VS) C# editor because of the deployment procedures. The executable program is prepared in VS, and it is transferred to the device by cable or internet IP.
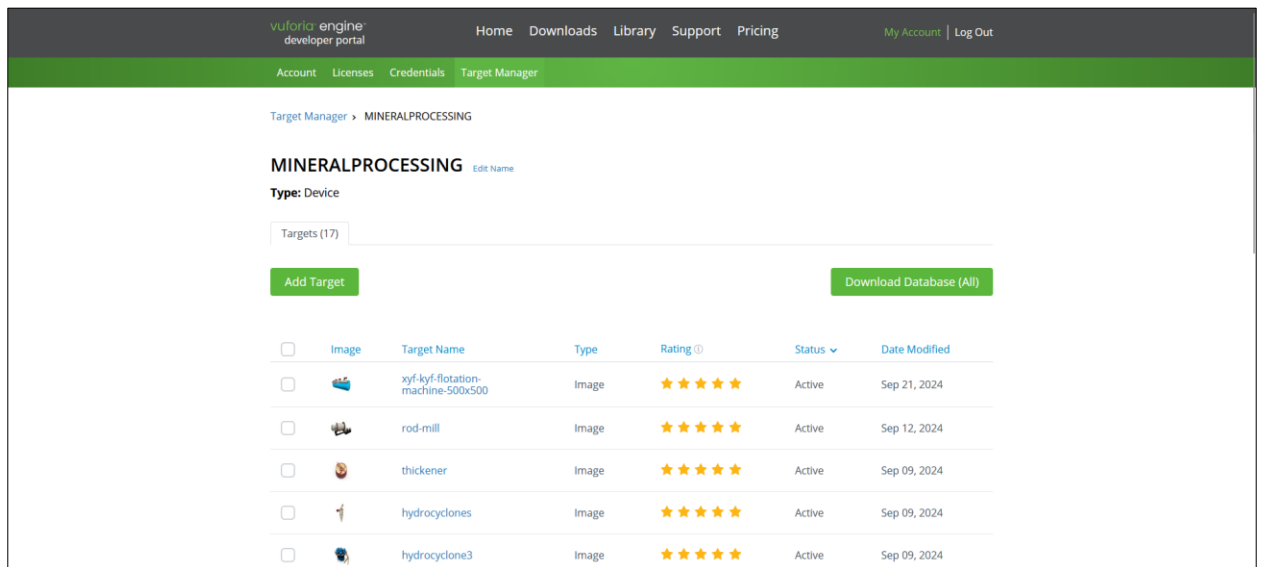
Fig.1. Vuforia Engine database for mineral processing machines.

Thus, the target images of the mobile device to be used as the AR camera have been defined (Fig.2a and 2b). The figures are shown here as they are to represent the editor where the applications are developed with their real outlook.

Fig. 2a. Unity scene designed for applications.

Fig. 2b. Various machines in the scene from another perspective.

The Image Target scene created with the MR Toolkit [24] in the Unity project was used for the second application. The difference between the first two applications, which are basically similar, is that the device on which the deployment will be made is the Hololens 2. Due to the nature of the application, the deployment process is a two-stage process. After the project is built in Unity, it is transferred to this device via the Visual Studio C# editor (Fig. 3).

Fig.3. Deployment to Hololens 2 from Visual Studio after building in Unity.

With the hand interaction components assigned to 3D models, in addition to the models appearing on image cards, operations such as drag, rotate, and scale can also be performed on them.

The third application was also developed for the Hololens 2 smart glass. For this ground plane type application, MR Feature Tool and MR Toolkit [6, 25] templates were used (Fig.4).
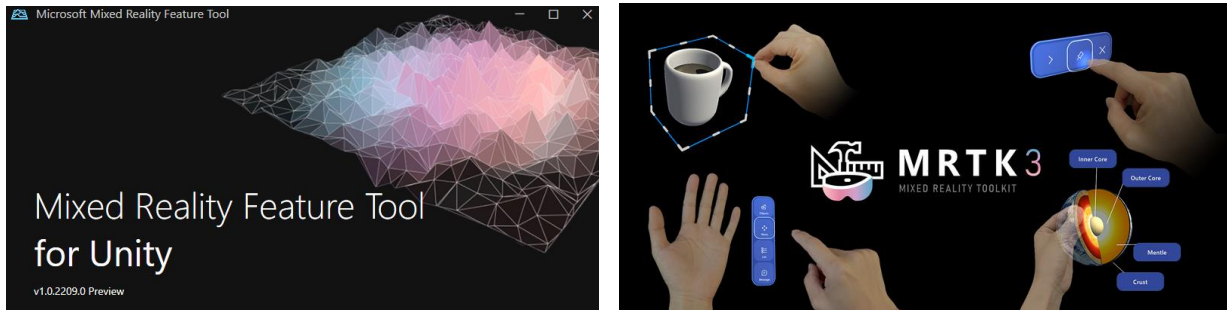
Fig.4. (a) MR Feature Tool for Unity; (b) Hololens 2 MRTK 3 templates.

Each machine in the Unity scene was assigned to the components below that would provide hand interaction controls:

- *Object Manipulator*
- *Bounds Control*
- *MinMax Scale Constraint*
- *MRTKUGUI Input Field or UGUI Input Adapter Draggable*
- *Box Collider*
- *Constraint Manager (if not included with Object Manipulator)*
- *NearInteractionGrabble.*

3. Mineral Processing AR Book and MR Applications

In the study, the fourteen most basic machines (Table 1) used in the size reduction and classification processes of mineral processing were used [43-56].

Table 1. Comminution and Classification Machines used in the project.

Comminution Machines		Classification Machines	
Crushers	Mills	Classifiers	Screens
Jaw Crusher	Ball Mill	Hydro-cyclone	Rotary Screen
Gyratory Crusher	Rod Mill	Spiral Classifier	Vibrating Screen
Cone Crusher	SAG Mill		
Impact Crusher			
Hammer Crusher			
Roll Crusher			

The AR Book database created in Vuforia was placed on the scene as Image Target cards in Unity. Figures 5 and 6 represent sample previews from the communication and classification pages in the AR Book, respectively. The 3D models matched with the Image Target cards were found in GrabCAD, Warehouse Sketchup, Rigmodels, and Sketchfab and were matched to shapes in the database.

JAW CRUSHER

It is a primary crusher. It consists of one movable and one fixed jaw.

They can break ores of any hardness.

Capacity: <1500 t/h

Maximum ore size to be fed: 0.8 - 0.9 x Mouth opening.

The proportion of larger ore that can pass through the throat opening: 15-20%

Size reduction ratio: 3/1 – 6/1

Breaker safety is provided by breaking the weak retaining arm.

Worn linings can be replaced.

Nominal size: Mouth width x mouth length (1800 mm x 2500 mm)

Vertical height = 2x Mouth opening

Max. feeding size: 1500mm

Max. outlet opening: 300 mm

Max. output grain size: 450 mm

Crushing type: Impact and compression

Settings: Throat opening, speed and amplitude adjustment

Power: 536 HP

Fig.5. An example page from the comminution machines part of the AR book [57-59].

HYDROCYCLONE

It consists of a cylindrical upper and a conical lower part with no moving parts.

a few mm to 2.5 meters in length,

Structurally CYLINDRICAL-CONICAL,

tangential feeding for its operation ,

Supply pressure: 30-35 kPa to 345-700 kPa, (5-50 psi)

Solid ratio in open circuit: 20-30%, in closed circuit: 60%

Feed size: 1-1.5mm to 45 microns (300 - 5 microns)

Capacity, large size: $25 - 30$ m^3/min.

Taper angle: 12 degrees (below 250 microns) − 20 degrees (above 250 microns).

Feed: $3.7 - 15$ m/sec (at feed inlet)

Size: Diameter: $4 - 80$ cm, height: $0.61 - 3.06$ m

Fig.6. Preview of a classifier machine page in the AR Book [57-59].

3.1. Augmented Reality (AR) Book Mobile Device Application

The first application of the study is the image target method for mobile devices. This application, developed for smartphones or tablets, has a quality that can be preferred in terms of accessibility for everyone. The scenario created by using Vuforia Engine was implemented. Some of the mobile device records are represented in Figures 7a and 7b.

Fig. 7. (a) AR video player plane for Jaw crusher and 3D model of a spiral classifier.

AR assets matched with the images are of three types in general such as 3D models, video players and animation. Three dots surrounded by a circle existing on the screen is called Device Options which include necessary setting controls for the user.
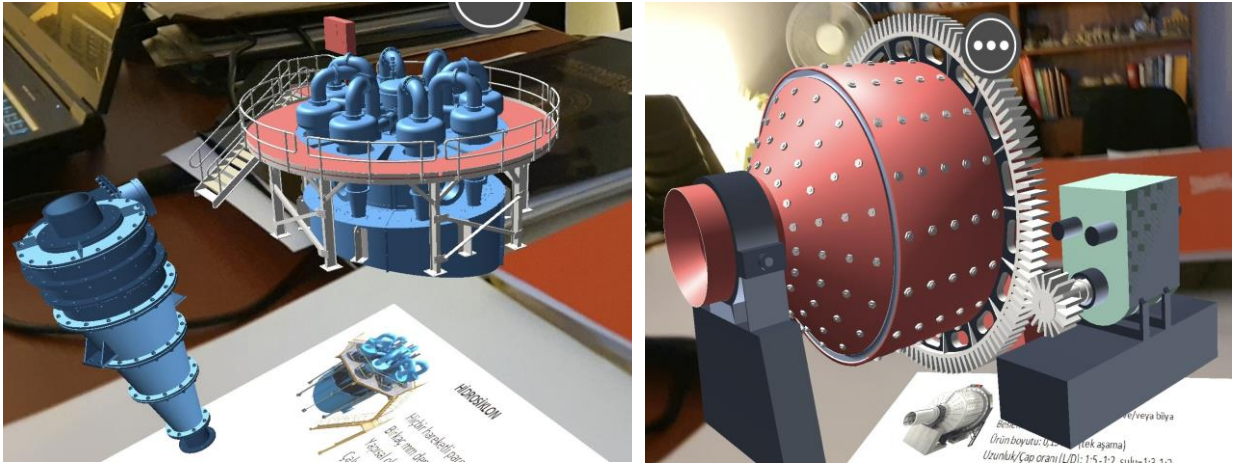
Fig.7. (b) Examples from AR Book Image Target application for mobile devices [28-42].

3.2. Image Target MR Smart Glass Hololens 2 application

In this application, the image target method was again preferred. Image cards were taken from the database previously created in Vuforia Engine. After the deployment process to Hololens 2 smart glass, models were displayed on the cards. In addition, all models are controlled with hand interactions such as drag, rotation, and scale. In this application, virtual designs were combined in a real environment, and the MR feature was experienced with hand control. The visuals of the study are in Figure 8.

Fig.8. Hololens 2 application with Image Targets scene use.

3.3. Ground Plane MR Smart Glass Hololens 2 Application

In this application developed for Hololens 2, models created in Vuforia Engine are displayed on the ground without being dependent on images, and all hand interaction operations can be performed. Some images of the work performed in the MR Toolkit (MRTK) [24] template are shown in Figure 9.

Fig.9. (a) AR view of the mineral processing machine group.
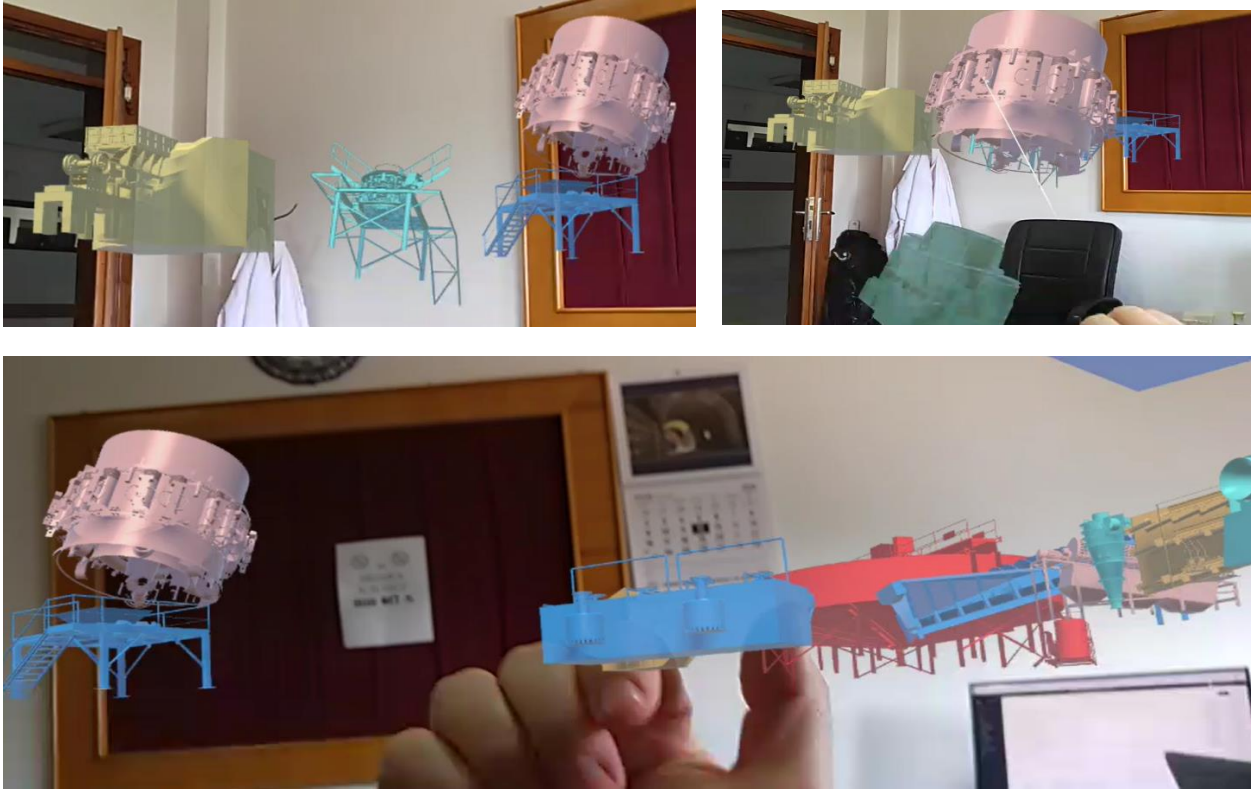
Fig.9. (b) Hololens 2 ground plane MR toolkit application.

The three applications that comprise the study were completed and tested this way. After the deployment process to Mobile and Hololens 2 hardware, it was opened for students to experience and evaluate.

4. Student Survey

The scope and aim of the questions are currently confined to measuring the instant perception of the students rather than a detailed statistical analysis. The course students are asked to assess the contribution of augmented reality applications to their training. The assessment was for three application frames:

1- Augmented Reality (AR) book (AR-Book) mobile device application
2- Image Target holographic head (Hololens-2) application
3- Ground Plane holographic head (Hololens-2) application

They are requested to write a score between 1 and 10 on the questions (Table 2).

Table 2. Template of the first group questions directed to the students for each application.

	QUESTION	POINTS (1-10)
1	I think knowledge is more retainable	
2	It contributes positively to learning	
3	Education becomes more enjoyable	
4	It contributes to the quality of education	

| 5 | It increases the interest in the course | |
| 6 | It would be beneficial if this application became more widespread | |

Finally, a comparison table was given to the students for a holistic evaluation of the three applications to be graded from 1 to 10 (Table 3).

Table 3. Template of the second question related to holistic grades of the approaches and their comparison.

1. AR Book mobile	2. Hololens-2 (Image-Target)	3. Hololens-2 (Ground Plane)

Before the students experienced these applications, a general explanation was made about the content, purpose and what was expected of them. They were asked if they had experienced this kind of experience in the lessons before. They stated that they had never experienced such a setup in any lesson. Then, they were given training on the devices and the use of the application.

Twenty students from various nations were selected from different classes who have taken the relevant courses. Three of the students were female, and seventeen were male.

4.1. First Group Questions for Assessment of Particular Applications

The first question group was directed at the students for the assessment of the AR Book Mobile case. The average values of the answers are shown in Figure 10.
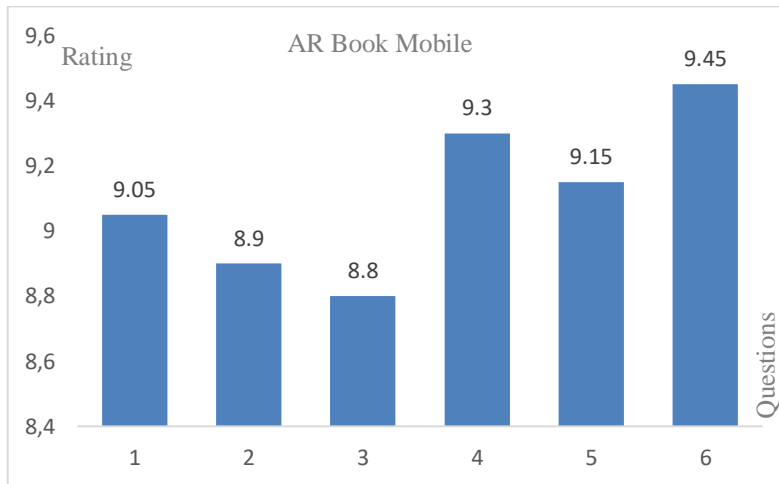
Fig.10. Assessments of the students for AR Book – mobile application.

The results show a positive perception of the application regarding grades ranging between 8.8 to 9.45. ANOVA Table of the student-question matrix is presented in Table 5.

Table 5. ANOVA Table for AR Book Mobile assessments.

Source of Variation	Sum of Squares (SS)	Degrees of Freedom (df)	Mean Square (MS)	F-Statistic (F)	P-Value
Between Groups	7.93	5	1.586	3.2868	0.0093

Within Groups	54.98	114	0.4823	
Total	62.91	119		

Here, the F-value, 3.2868, suggests that the variation between the groups (differences in scores for different questions) is moderately greater than the variation within the groups. This indicates that there are notable differences in scores across the questions. The P-value 0.0093 is quite below the typical significance level of 0.05, which means that the probability of the observed differences occurring by chance is quite small. Therefore, we can conclude that the differences between the questions are statistically significant.

The second question group was for the assessment of the AR Book Hololens 2 (image target) case. The average grades regarding the answers are shown in Figure 11.
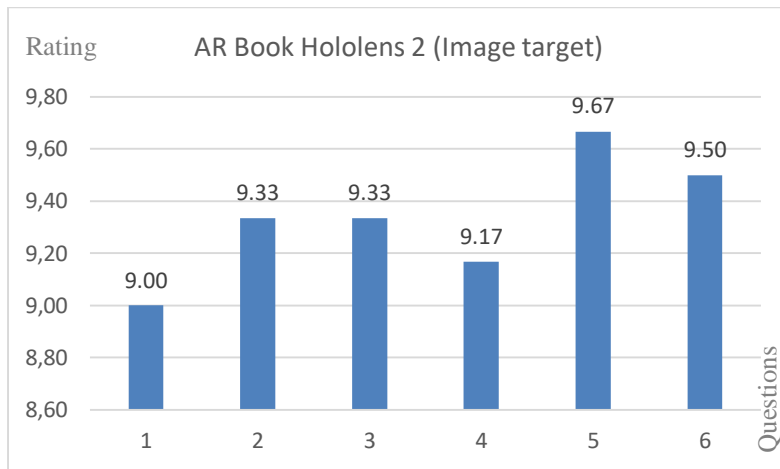
Fig.11. Assessments of the students for AR Book – Hololens 2 case.

Here, there is an obvious increment in the grades relative to the mobile case. The grades range between 9.0 to 9.67 which shows a better contribution of Hololens 2 application on AR Book images. ANOVA Table (Table 6) supports this graph.

Table 6. ANOVA Table for AR Book Hololens 2 (Image target) assessments.

Source of Variation	Sum of Squares (SS)	Degrees of Freedom (df)	Mean Square (MS)	F-Statistic (F)	P-Value
Between Groups	3.87	5	0.774	3.0338	0.0126
Within Groups	29.1	114	0.2553		
Total	32.97	119			

The F-value 3.0338 expresses that the variation between the groups (differences in scores for different questions) is moderately greater than the variation within the groups, which indicates the notable differences in scores across the questions. The low value of P 0.0126 differences between the groups are statistically significant.

The third case was the Hololens 2 Ground Plane application. Here, all the machines exist at the same time on the ground and cause some decline in the speed of interactions. So, the grades are slightly less than in the previous case. This is due to control difficulties, sometimes interruptions and breaks. However, this is a relative decrease in

comparison to others and particularly, in total, the grades are still satisfactory. The positive thinking of the students exists in the ranges from 7.83 to 9.0 (Fig.12).
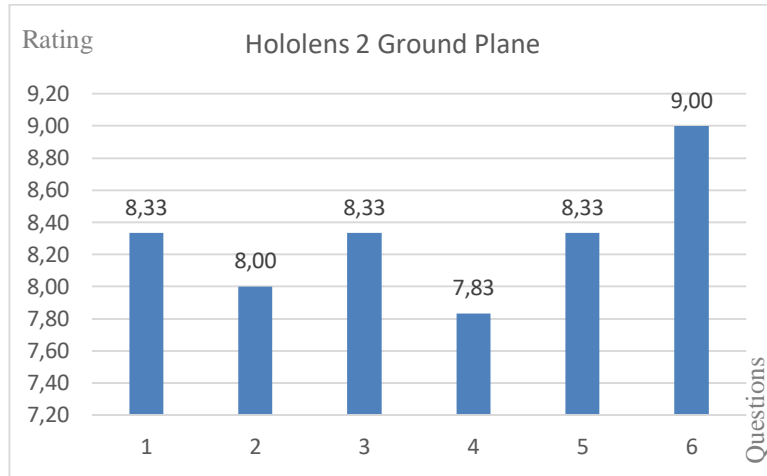
Fig.10. Assessments of the students for (a) AR Book – mobile, (b) AR Book Hololens 2, and (c) Ground Plane Hololens 2

Besides, the ANOVA Table (Table 7) points out that the variation between the groups (differences in scores for different questions) is much greater than the variation within the groups and significant differences in scores across the questions with an F-value of 9.09. Also, 0.000001 P-value is so low P-value and indicates that the probability of the observed differences occurring by chance is very small.

Table 7. ANOVA table for Ground Plane Hololens 2 assessments.

Source of Variation	Sum of Squares (SS)	Degrees of Freedom (df)	Mean Square (MS)	F-Statistic (F)	P-Value
Between Groups	61.2	5	12.24	9.09	0.000001
Within Groups	125.7	114	1.103		
Total	186.9	119			

Considering the 100% scale, maximum average grades and their application types can be listed according to the student's assessments:

    i. knowledge will be more retainable (90.5%, AR Book Mobile),
    ii. it contributes positively to learning (93.3%, AR Book Hololens 2),
    iii. education becomes more enjoyable (93.3%, AR Book Hololens 2),
    iv. it contributes to the quality of education (91.7%, AR Book Mobile),
    v. it increases interest in the course (96.7%, AR Book Hololens 2),
    vi. it would be beneficial if this application became more widespread (95%, AR Book Hololens 2).

4.2. Holistic Comparison of the Three Applications

In the second feedback table, they were asked to evaluate the AR applications they experienced from a holistic

perspective and rate them between 1 and 10 (Fig.11). Here, the purpose is to get an immediate idea about which application provides better influence and contribute to the training experience. All the questions were directed after the practice in the class to understand the immediate reaction of the students. So, both the first group questions and the second holistic question aim to measure this application.
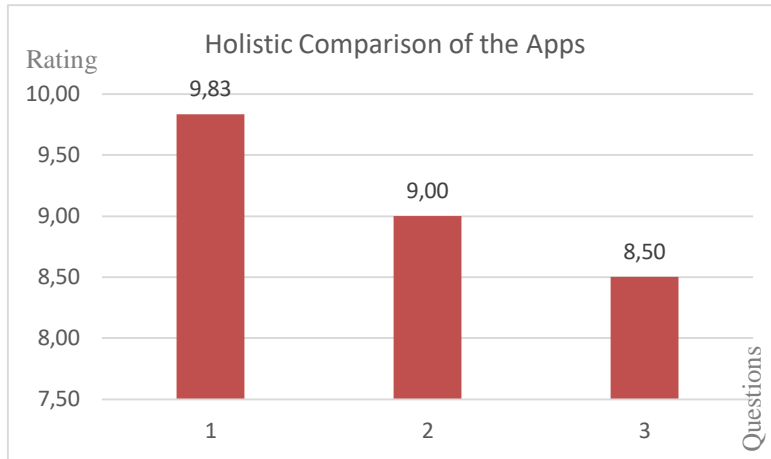
Fig.11. A holistic assessment of the students for the applications.

Students stated that they mostly found Hololens 2 visually superior and impressive and made the evaluations in the first tables from this perspective, as seen in Figures 8 to 10. However, they verbally stated that they prioritized accessibility and applicability in daily education when evaluating the applications holistically. In this respect, they concluded that the mobile application was preferable with 98.3%. ANOVA Table related to this assessment is given in Table 8.

Table 8. ANOVA table for Holistic assessments.

Source of Variation	Sum of Squares (SS)	Degrees of Freedom (df)	Mean Square (MS)	F-Statistic (F)	P-Value
Between Groups	14.63	2	7.315	7.5587	0.0012
Within Groups	53.75	57	0.942		
Total	68.38	59			

Accordingly, the F-value of 7.5587 indicates that the ratio of the variance between the groups to the variance within the groups is relatively high, which points out that the differences between the applications are more substantial than the variations within the applications. The P-value of 0.0012 is much lower than the typical significance level of 0.05. This strongly suggests that the differences between the means of the three applications are statistically significant.

5. Conclusion and Recommendations

In this research, a study was conducted in which AR Book and mixed reality applications were developed with smartphones and Hololens 2 in the training of mineral processing machines, which has not been done before, and the effects on education were evaluated by the students after the traditional education. In other words, the study investigated the contribution of augmented reality (AR) and mixed reality (MR) applications to the traditional training

of mineral processing machines, including some of the comminution and classification ones. For this purpose, two image targets and a ground plane application were developed by using Unity and Vuforia engines. Image target applications in AR Book format were designed for smartphones and MS Hololens 2, a mixed-reality device. The ground plane application was implemented for Hololens 2.

For the image target-based part of the study, a visual database for communication and classification machines was created in the Vuforia AR engine and converted into a Unity package. An asset folder was created with 3D models for all machines and videos simulating the working systems for some machines. Image cards, 3D models and videos were matched in the Unity editor. Smartphone and Hololens 2 were determined as the AR cameras required for the application. The created application files were deployed to Android phones and the Hololens 2 disk.

The booklet designed for communication and classification machines was transformed into an AR Book with the use of smartphones and Hololens 2. In other words, the applications were triggered with the images in the booklet, 3D models and videos were created virtually in the book and the machines were visualized in 3D and hand interaction in a real environment. It was also possible to obtain hand interaction on smartphones with the Lean-Touch component. Since the Hololens 2 device already has standard AR and MR features, both AR and MR applications were performed. The first of these applications was an AR Book, and the other was a ground plane application that did not need to trigger a book.

Regarding all feedback, it can be concluded that the training supported by AR and MR applications provides more retainable and memorable knowledge. It contributes to learning positively; education becomes more enjoyable. AR and MR contribute to the quality of teaching and increase interest in the course, and it would be beneficial if their application became more widespread.

This study is a basic study used to ensure that some machines used in the field of Mining Engineering-Ore preparation are taught to students better and more effectively with AR technologies. In this context, AR application for mineral processing machines can be considered as a complementary study.

Additionally, AR technologies can also be used in education and training in the following cases:
- Use of these machines in process stages in facilities.
- Disassembly and assembly of these machines.
- Occupational health and safety for these machines or in facilities
- Operation and maintenance of these machines.
- Use of AR and MR technologies in all relevant disciplines of engineering, natural science, architecture, historical places and education-related activities.

Acknowledgments

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RESEARCH ARTICLE

The relationship of cathepsin-k level with some biochemical and hematogical variables in women with osteoporosis, pregnant and menopausal

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Abstract

In this study, the biochemical and hematological variables in 180 patients (women) between 17 and 75 years old were hospitalized at Al-Sadr Teaching Hospital in Najaf Iraq between April and July 2023. The patients were devised in 4 different group studies with 180 patients in each group consisting of 45 women: female with osteoporosis in the range age 22-35, a pregnant female in range age 17-37, female menopause range age 45-75, and healthy females in range

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age 19-65 as the control group. The biochemical variables such as level of Cathepsin K (Cath-k) concentration, Estradiol (E2) concentration, vitamin D (Vit -D), and parathyroid hormone (PTH) concentration in women with osteoporosis, menopause, pregnant and healthy women were evaluated. In addition, the hematological variables: red blood cells (RBCs), hemoglobin (Hb), hematocrit (HCT), number of platelets (PLT), and number of white blood cells (WBCs) were evaluated in different study groups. Also, the concentration of phosphate (P) and Body Mass Index (BMI) was estimated. In the end, the correlation test with each variable in different group studies was calculated by the STATISTICA program. The obtained results showed that there was a significant increase in the numbers of WBCs, the concentration of Cath-k, PTH, and BMI for the study groups compared to the control group, as well as a significant decrease in the concentration of P and Vit -D for the study groups compared to the control group. There is a significant increase in the E2 hormone in the group of pregnant women and a significant decrease in women with osteoporosis who are in menopause compared to the control group, as well as the presence of a significant decrease in RBCs, and Hb in the group of pregnant women compared to the control group. There is a significant increase in the numbers of PLT in the group of women with osteoporosis and women in menopause compared to the control group, as it is concluded from the current study that there is a close correlation between some different variables, including a good correlation between BMI and PLT was found to be 0.83. This may confirm that BMI is associated with increased cardiovascular morbidity and mortality through various molecular mechanisms possibly linking metabolic syndrome to hemostatic and vascular abnormalities in addition, a good correlation was observed between PTH and Cat-k (0.89), which indicated there is a relation between these two parameters.

1. Introduction

According to the WHO definition, osteoporosis is a generalized skeletal disease, characterized by low bone density and alterations in bone microarchitecture, responsible for excessive bone fragility and therefore a high risk of fracture [1]. This pathology particularly affects women aged 50 and over. In France, 3 million people are affected. It is a disease that is constantly increasing around the world but more particularly in Europe, linked to the increasing aging of the population. Osteoporosis is a serious disease, poorly understood by most patients, although established knowledge has recently emerged [1].

The severity of osteoporosis is directly linked to the consequences caused by osteoporotic fractures. Indeed, these fractures often compromise the quality of life of patients with an increase in morbidity. Patients often present with chronic pain, impaired mobility, increased disability, and dependence. To a greater degree, osteoporotic fractures are also responsible for an increase in mortality, especially in the first year following the fracture [2].

Early therapeutic management of osteoporosis could considerably reduce the cost generated by this disease (hospitalizations, long-term care at home, institutionalization in expensive adapted structures, etc.). Currently, this treatment is too insufficient, to the point that only around 20% of patients benefit from it after a fracture. The management of this disease thus becomes a public health objective set by the law of August 9, 2004 [3].

Cathepsin K (Cath-k) was recently proposed as a possible alternative bone marker [4]. Cath-k is a cysteine protease that breaks down type I collagen in bone through the action of osteoclasts [5]. It was discovered that mutations in the Cath-k gene cause pycnodysostosis, an autosomal recessive bone sclerosing condition [6]. On the other hand, Cath-k overexpression in osteoclasts sped up the trabecular bone turnover in mice [7]. In addition, in nonhuman primates, suppression of human Cath-k inhibits bone resorption in vivo [7].

Osteopetrosis is caused by decreased osteoclastic bone resorption in mice missing Cath-k, as shown by Saftig et al. [7]. Cath-k may be a helpful and precise biochemical marker of osteoclastic activity as it is produced and secreted by osteoclasts during active bone resorption.

According to Henriksen et al.[8], circulating levels of Cath-k can be utilized as a surrogate measure of osteoclast number since they are equal to the total amount of osteoclasts. The qualification of Cath-k serum levels in the diagnosis

of osteoporosis is examined in this study. Serum Cat-k may be helpful in detecting postmenopausal women with osteoporosis, according to several researchers who have reported increased levels of this protein in osteoporotic people [9][10].

This study aimed to evaluate the biochemical and hematological variables in patients women between 17-75 years old hospitalized in hospitalized at Al-Sadr Teaching Hospital in Najaf , Iraq between April and July 2023, Iraq between April, and Jully 2023. The patients were devised in 4 different group study with 180 patients in each group consist of 45 women: Female with osteoporosis in range age 22-year, Pregnant female in range age 17-37, Female menopause range age 45-75, and Healthy females in range age 19-65. The biochemical variables such as level of Cath-k concentration, estradiol (E2) concentration, vitamin D (Vit -D) and parathyroid hormone (PTH) concentration in women with osteoporosis, menopause, pregnant and healthy women was evaluated. In addition, the hematological variables: red blood cells (RBCs), hemoglobin (Hb), and hematocrit (HCT), number of platelets (PLT) and number of white blood cells (WBCs) were evaluated in different study groups. Also, the concentration of phosphate (P) and Body Mass Index (BMI) was estimated. In the end the correlation test with each variable in different group study was calculated by STATISTICA 10.0 program.

2. Materials and Methods

2.1. Study design

In this work the biochemical and hematological variables were evaluated in patients between 17-75 years old hospitalized Al-Sadr Teaching Hospital in Najaf, Iraq between April and Jully 2023.

The patients were devised in 4 different group studies with 180 patients in each group consisting of 45 women: females with osteoporosis in the range age 22-35, pregnant females in range age 17-37, females with menopause range age 45-75, and healthy females in range age 19-65 as the control group.

BMI was estimated. The correlation test with each variable in different group studies was calculated by the STATISTICA program.

2.2. Blood collection

Venous blood samples were obtained in the sitting position by using a disposable syringe (5 mL). Five ml of blood was obtained from each person by piercing the vein and slowly pushing it into two tubes (3 mL blood in the plan tube and the other 2 mL blood in the EDTA tube for CBC). The plane tube was centrifuged for 10-15 minutes at a speed of $(10,000 \times g)$ then the serum was divided into two parts and stored at -20˚C until analysis.

2.3. Evaluation of hematological variables

A blood test was performed on all patients in the group studied by collecting venous blood samples after a fast of more than 8 hours, as well as WBCs, RBCs, Hb, HCT, PLTs were tested. Blood tests were measured using the LABGEO PT 9 liver test (Samsung Electronics).

2.4. Evaluation of biochemical variables

2.4.1. Determination of E2-level
To prepare the reagent, the wash solution was diluted with distilled water the 1:20. Enzyme conjugate was prepared by adding the contents of the bottle (25 ml) to 475 ml of distilled water. Solutions were stored at room temperature. All reagents and samples were brought to room temperature before starting. Then volume of 25 µL of standard, specimens and controls was added to the appropriate wells, and a volume of 50 µL of working solution of Estradiol Biotin Reagent was added to each well and was mixed well by placed on a shaker for 20 seconds. Then plate was covered and incubated for one hour at 25 ºC. After that, a volume of 100 µL of Estradiol Enzyme Reagent was added

to all wells and mixed well by placing them on a shaker for 20 seconds and then incubated for 45 minutes at 25 ºC. The microplate was discarded from the solution and washed using 300 µl wash buffer three times, a volume of 100 µl of tetramethyl benzyl (TMB) reagent was added to each well and incubated for 20 minutes at 25 ºC. A volume of 50 µl of stop solution was added to each well for topping solution. Then the microplate contents were mixed gently for 30 seconds to make sure that all the blue color changed to yellow color completely. The absorbance of each well was determined at 450 nm with a microplate reader within 15 minutes after adding the stop solution.

2.4.2. Determination of Vit -D in Blood Serum
Vit -D was estimated in the blood serum using the ready-made kit from the Chinese company BIONT, by following the steps attached to the kit, and using the ELISA technique. The detailed experiment was mentioned in support information.

2.4.3. Determination of PTH levels
PTH levels were determined using ELISA technique according to the kit procedures.

2.4.4. Determination of Human Cat-k Levels
Cat-k levels were determined the spectrophotometric method. For the standard solution, a volume of 120 µL of the standard (16 ng/ml) was diluted with 120 µL of standard diluent to generate an 8 ng/mL standard stock solution. The standard solutions were allowed to sit for 15 minutes with gentle agitation prior to making dilutions. A volume of 50 µL standard was added to standard wells, then a 40 µL of serum was added to sample wells then 10 µL of anti- Cat-k antibody was added to sample wells. A volume of 50 µL of streptavidin-HRP was added to sample wells and standard wells and mixed well, then the plate was covered with a sealer and incubated for 60 minutes at 37 ºC. The sealer was removed, and the plate was washed 5 times with 0.35 mL of wash buffer, 50 µL of substrate solution A was added to each well, and then 50 µL substrate solution B was added to each well and the plate was incubated after covering with a new sealer for 10 minutes at 37 ºC in the dark. A 50 µL of stop solution was added to each well, and the tube color changed from blue to yellow immediately. The absorption was determined of each well using a microplate reader set at 450 nm within 10 minutes after adding the stop solution.

2.4.5. Determination of P concentration in blood serum

P concentration in blood serum was determined by spectrophotometric method. The principle of the method is based on the reaction of phosphate in serum with ammonium molybdate and changing color. Color intensity was measured at 340 nm and calculated in mg/dL by comparison with the standard curve.

2.5. Statistical analysis

The statistical study based on patient responses transcribed in the form of an Excel table. The ANOVA TEST was used to find the arithmetic mean and standard deviation, and the correlation test was determined. Qualitative variables were obtained and compared using the Fischer exact test. The chosen threshold of statistical significance was $p < 0.05$, i.e. a risk of concluding that there was an inaccurate difference between groups.

3. Results and Discussion

3.1. Standard curves

3.1.1. E2 level
The standard curve is generated by plotting the absorbance obtained for each reference standard on the vertical axis (Y) against the corresponding concentration (pg/ml) on the horizontal axis (X). Figure 1a. shows the absorption values for each sample versus the corresponding E2 concentration of the standard curve.

3.1.2. Human Cat-k Levels

A standard curve was created by plotting the absorption of standard solutions on the vertical (y) axis versus their concentration on the horizontal (x) axis. Test concentration was calculated by drawn an appropriate curve and by point to point on the graph.as shown in Figure 1b.

3.1.3. Vit -D in blood serum

The rates of the optical absorption values were calculated for each group, then a curve was drawn by means of the absorption rate that is obtained from each measurement against its concentration, as the absorbance is on the vertical Y axis and the focus is on the horizontal X axis, as shown in the Figure 1. Then the absorbance values decreased to the values obtained from the samples on the curve showing the hormone concentration (pg/mL).
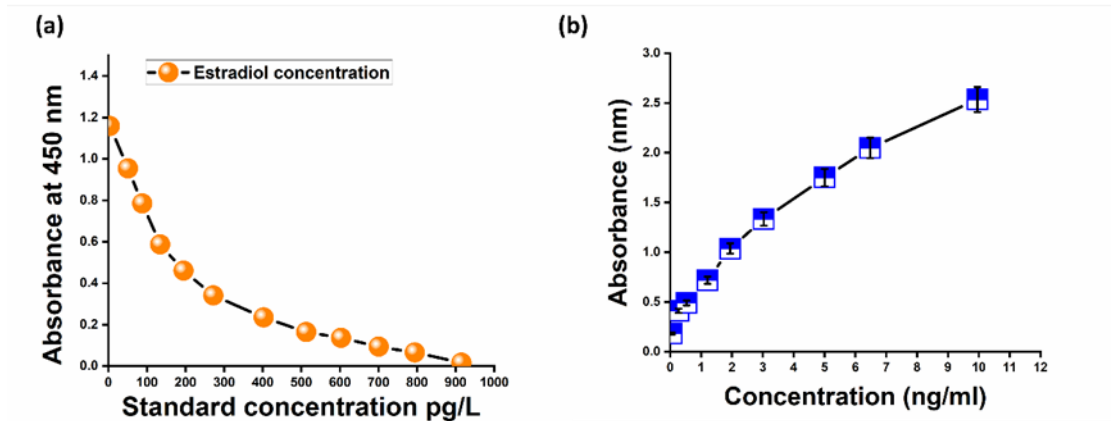

Fig 1. (a) The standard curve of E2 and (b) standard curve of the concentration of Cat-k.

3.2. Statistical analysis

3.2.1. Level of biochemical variables in blood serum

The results of the Cath-k level in different study groups were illustrated in Figure 2(a) and showed significant results ($p>0.05$). The increase in the activity of the Cath-k enzyme in the study groups of women was observed, which includes each of the pregnant women group, groups of menopausal women, and the group of women with osteoporosis, and the values were respectively (0.24 ± 11.50, 12.73 ± 0.17, 11.99 ± 0.15) compare with a healthy woman (blank) (3.95 ± 0.01) while decrease activity Cath-k level in pregnancy group compares in menopause group and osteoporosis group for woman this obtained results are compatible with reference study [11].

A study shows that the Cat-k enzyme is associated with estrogen in an inverse relationship with respect to the effect on bone metabolism, and the decrease in estrogen concentration in postmenopausal women and young women who suffer from a decrease in the hormone for several reasons, including those related to polycystic ovaries, have an increase in the activity of the Cat k enzyme due to the weak protective effect of estrogens on bones, as they increase bone resorption in reducing the number and activity of osteoblasts and accelerating programmed death [11]. An other study shows that the increased activity of the Cat-k enzyme during menopause in women is the result of their hyperparathyroidism, knowing that the high concentration of PTH and its catabolic effect on bones led to an increase in the effectiveness of the Cat-k enzyme in them and an increase in their incidence of fractures [12]. According to Adami and his colleagues, drugs might sometimes be the primary factor contributing to the detrimental effects on bones, making them more brittle and susceptible to breakage. Patients on glucocorticoids have higher levels of Cat-k enzyme because the drug's side effects have increased osteoporosis rates. These side effects include increased osteoblast cell programmed death and inhibition of osteoblast progenitor cell formation, while osteogenic cell secretion of Cat-k has increased [13].

The concentration of Vit-D in blood serum in different groups presented was shown in Figure 2(b). A significant decrease in Vit -D levels was observed in the groups of women, which include both the group of postmenopausal women, pregnant women, and the group of women with osteoporosis and the values were as follows (12, 75 ± 2.81), (11.94 ± 2.52), (7.88 ± 2.48) compared to the Vit -D level in healthy women groups (34.62 ± 4.64). The results obtained showed that the rate of Vit -D levels in osteoporosis groups is lower compared to women. at menopause, pregnant women. The obtained results are compatible with other references [14]. Vitamin D deficiency in pregnant women can be caused by decreased calcium, and this decreased calcium is due to the high need of the fetus to build its skeleton, especially during the last trimester. During pregnancy, if the mother does not obtain adequate calcium requirements, the mother`s body withdraws calcium from her bones and provides it to the fetus, but the persistence of the deficiency without treatment is a dangerous factor for the fetus during its growth and its long-term negative effects, even after birth, result in increased susceptibility to diseases, including rickets and diabetes [15]. In this work, Adit et al. demonstrate that adolescent pregnant moms had greater rates of osteoporosis and bone density loss than their peers, and that the age of the pregnant woman may be a significant factor in vitamin D shortage equivalents throughout puberty to expectant mothers [16]. The primary cause of osteoporosis in postmenopausal women is the decline in ovarian function and menopause, as well as the low level of vitamin D in them. The interruption causes a decrease in skeletal mass due to an imbalance in bone metabolism because the decline of ovarian functions is the most important factor in the development of osteoporosis after menopause. In postmenopausal women, the decrease in vitamin D is explained by the low consumption of milk and dairy products, the high percentage of body fat, the lack of sun exposure, and the significantly lower concentration of estrogens [17].
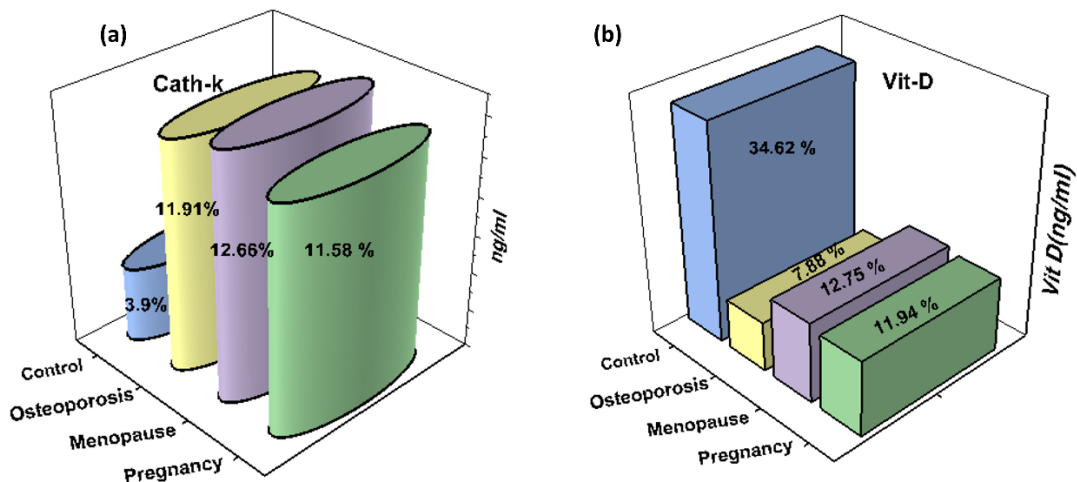
Fig 2. (a) The evaluation of Cath-k level and (b) level of Vit -D in different group study.

The Figure 3a, and b illustrates the concentration of E2 hormone and PTH hormone in different study groups respectively. The concentration of E2 hormone decreased significantly in the menopausal and osteoporotic women groups and the concentrations were found to be 28.39 ± 6.46 and 51.11 ± 10.55, respectively. The results are shown in Figure 3b. On the other hand, a significant increase in the E2 hormone was observed in the pregnancy group (416.85 ± 38.35) compared to the control group (277.75 ± 78.61), so the results obtained from the study approved a significant increase in the E2 hormone in the pregnancy group. in relation to menopause and women suffering from osteoporosis. The obtained results are compatible with other studies [18]. The studies indicated that osteoporosis occurs in both sexes and all age groups and races, but it is found higher in women After menopause, due to estrogen deficiency, the onset of cell aging, decreased immunity, increased inflammation within the body, medication intake, calcium and vitamin D deficiency, and an increase in thyroid hormones [19].

In addition, the estrogen deficiency increases the secretion of interleukin IL-6, interleukin IL-1, and tumor necrosis factor-α- TNF and thus the occurrence of bone resorption, as the lack of estrogen works to reduce the work of osteoblasts and increase the activity of osteopenia, which leads to the removal of minerals and the occurrence of osteoporosis after menopause. During pregnancy, the concentration of the estrogen hormone rises to levels much higher than the normal limit, and for several reasons [20].

Calc-spar et al. [19] indicated that during pregnancy the mammary glands undergo a series of structural and functional changes to prepare for milk production, as there are three hormones that have a major role in the development of tissue in the breast. The breast gland, which is estrogen, progesterone, and prolactin, as estrogen mainly works to promote and develop the lactiferous duct and prepare it until milk comes out after childbirth. It stimulates the secretion of the prolactin hormone and increases the receptors for this hormone in the breast glands [21]. A study by Winter et al. showed that the protective effect of estradiol on the bones decreases during pregnancy and lactation, which causes weakness in building new bone cells, and during the lactation period, the rise in prolactin causes a decrease in bone minerals[22].

The results of PTH levels in different groups of study are illustrated in Figure 2b. According to the study results, a significant increase in PTH concentration was observed in all female groups. The value of PTH hormone was found to be 111±1.23 in the pregnant women group, 95.46±1.36 in the group of menopausal women, and 88.14±2.32 in the group of women with osteoporosis compared with the concentration of PTH hormone in the control group (58.11±2.32). Where the results showed that there was a significant decrease in the concentration of PTH in groups of pregnant and menopausal women, compared with women with osteoporosis. This results are compatible with other references [23]. PTH regulates calcium balance by acting on many body organ systems in order to maintain a normal blood calcium concentration, while high levels of the hormone that occur due to low blood calcium concentration cause bone resorption and may be due to increased PTH in women with osteoporosis[24]. According to Bover et al.[25], Vitamin D deficiency is caused by either inadequate nutrition or lack of exposure to sunlight, which results in a lack of calcium in the blood. In response to this deficiency, more hormones are secreted. When vitamin supplements prescribed by the attending physician are taken, the concentration of vitamin D in the body and, accordingly, the hormone concentration return to normal values.
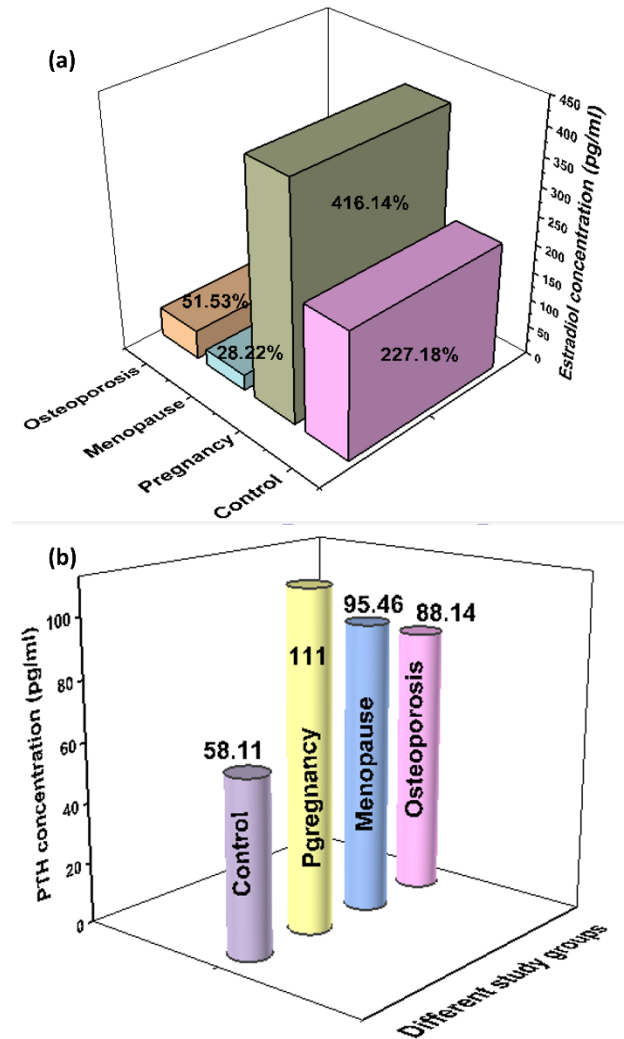
Fig 3. (a) Level of E2 and (b) level of PTH in different group study.

3.2.2. Determination of the Hematological profile in the study groups.
Concentration of RBCs, Hb, and HCT

The results obtained for the number of RBCs, Hb, and HCT in the different study groups are illustrated in Figure 4. A significant decrease in the number of RBCs, Hb, and HCT in the group of pregnant women, and the values were respectively: $(4.29 \pm 0.52, 34.60 \pm 0.42, 11.20 \pm 0.26)$ compared to the control groups $(4.76 \pm 0.95, 12.53 \pm 0.4, 37.79 \pm 0.83)$ Although no significant differences appeared in the two groups of postmenopausal women and women with osteoporosis compared to the healthy group of women (control group). A decrease in RBCs and Hb and HCT concentration was observed in the group of pregnant women, compared to both groups of postmenopausal women and those with osteoporosis.

The number of RBCs can decrease for several reasons, including genetic (hereditary) and others due to acquired (non-hereditary) diseases. This decrease affects the course of vital processes in the body as a whole because cells contain the protein hemoglobin, which carries oxygen to all cells of the body to produce energy when the number of RBCs

decreases. Hb and HCT (the percentage of RBCs in whole blood) will be affected, and therefore anemia.
Iron deficiency anemia is the most common nutritional deficiency, which the World Health Organization has highlighted as a serious health problem not only in developing but also in developed countries. Anemia is estimated to affect approximately one-third of the world's population, particularly women of childbearing age. One of the global nutrition goals set by the organization that must be achieved is to reduce the number of anemic women by 50% [26]. During pregnancy, the volume of blood increases for the growth of the fetus, but if the pregnant woman does not get enough iron or some other nutrients, the body's organs will not be able to produce enough RBCs that the mother and her fetus need, and thus she will suffer from anemia, which is one of the most common medical disorders during pregnancy Where the World Health Organization indicated that 60% of pregnant women will develop anemia, and the most vulnerable women are those with limited incomes and adolescent girls [27]. There is a correlation between vitamin D and iron, as some studies indicated that osteoporosis (vitamin D deficiency) causes anemia in some other studies, and other studies indicated the opposite, where anemia causes osteoporosis, as vitamin D plays an important role in the formation of blood cells, Erythropoiesis, which is the process of producing RBCs from within the bone marrow [28].
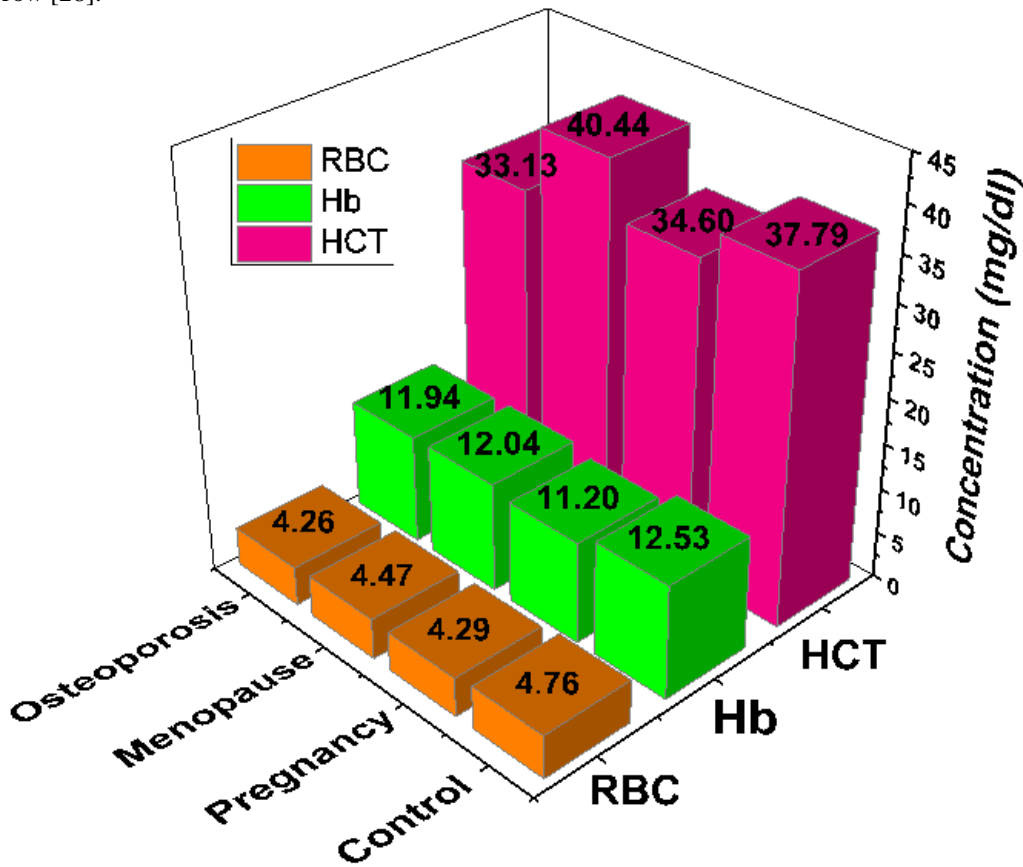
Fig 4. Concentration of RBCs, Hb, and HCT in different study groups.

Level of WBCs and the number of PLTs
The number of WBCs and the number of PLTs in the study groups of women were evaluated and the obtained results are shown in Figure 5. A significant increase in the number of WBCs in the study groups of women was observed, which includes each of the two groups of pregnant women, the group of menopausal women, and the group of women

with osteoporosis. The values were respectively (9.93±0.04, 8.64±0.21, 8.44±0.08) compared with the control group (7.95±0.02).

The results of PLTs showed a significant increase in the number of PLTs in the study groups of women, which includes each of the two groups of menopausal women, and the group of women with osteoporosis. The values were respectively (256.29±75.51,254.60±60.27) while the pregnant group of women did not show any significance in the number of PLTs (241.31±51.65) compared with the control group (242.38±70.92).

A study showed that blood cells are used as inflammatory markers to describe many diseases, including osteoporosis, and indicated that people with osteoporosis had high levels of granulocytes and non-granular WBCs with low counts. Elevated platelet at higher levels than their peers without osteoporosis. Because osteoporosis is characterized by a defect in bone metabolism which is more in bone resorption than in its structure, and during this process, inflammatory cytokines will be involved. It promotes, develops, and increases the number of osteoporosis, thus reducing bone mineral density and accelerating its catabolism[29].

In postmenopausal women, the decrease in estrogen plays a role in increasing the inflammatory process of their bones, as the researcher Kale et al. [29] indicated that with the decrease in the concentration of estrogen and the presence of indicators of a decrease in bone density, an increase in WBCs has been observed during menopause and loss of the protective effect of estrogen on bones.

It is normal for there to be an increase in the number of WBCs in pregnant women due to the physiological stress resulting from pregnancy, as well as to protect the body against microbes and fight certain diseases that some pregnant women may suffer from, such as urinary and genital tract infections and arthritis, as well as to prevent blood clots and help widen blood vessels when exposed to allergies [30].
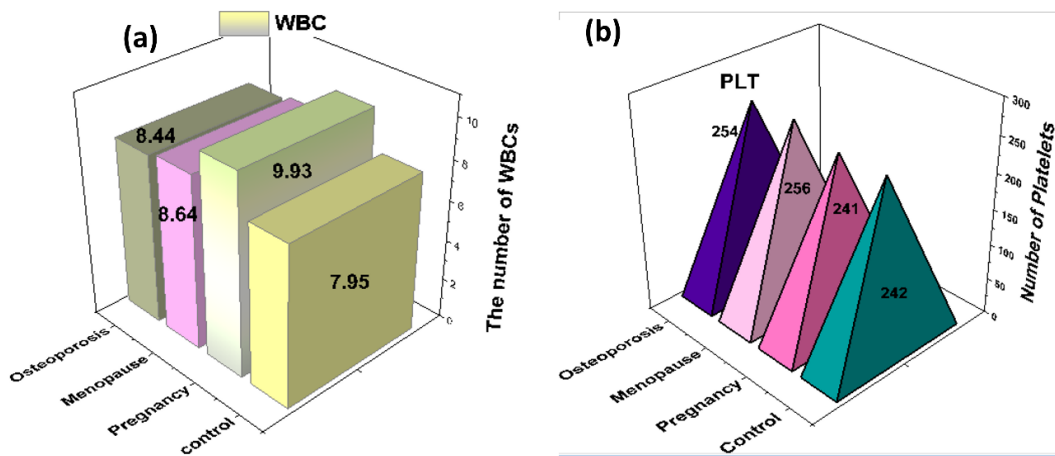
Fig 5. (a) Number of PLTs in different study groups and (b) number of WBCs in blood serum of different groups.

The concentration of P in the blood serum and BMI of the study groups
Figure 6 showed a significant decrease in the concentration of P in all groups of women, including each of the pregnant women group, the group of menopausal women, and the group of women with osteoporosis. The values were respectively (1.48 ±0.55, 1.42±0.91 and 2.05±0.49) compared with the control group (5.04±4.56). The results of the current study do not show any significance in all groups of women.

The reason for the decrease in phosphorus may be due to a deficiency of vitamin D, as all the researchers pointed out by Safari and Goltzman [31][32], Vitamin D has the optimal role in the absorption of both phosphorus and calcium through the intestines and re-absorption through the renal tubules. In case of deficiency, the concentration of both elements will be affected in a negative way.

Some studies have indicated the cause of low phosphorus and the occurrence of bone diseases as a result. It may be a defect in the activity of FGF-23H or PTH, as they work together to regulate the concentration of phosphorus in the

blood serum. The production of FGF-23H by osteoblasts and osteoblasts In response to an imbalance in the concentration of phosphorus in the blood to be regulated within normal levels [33] .
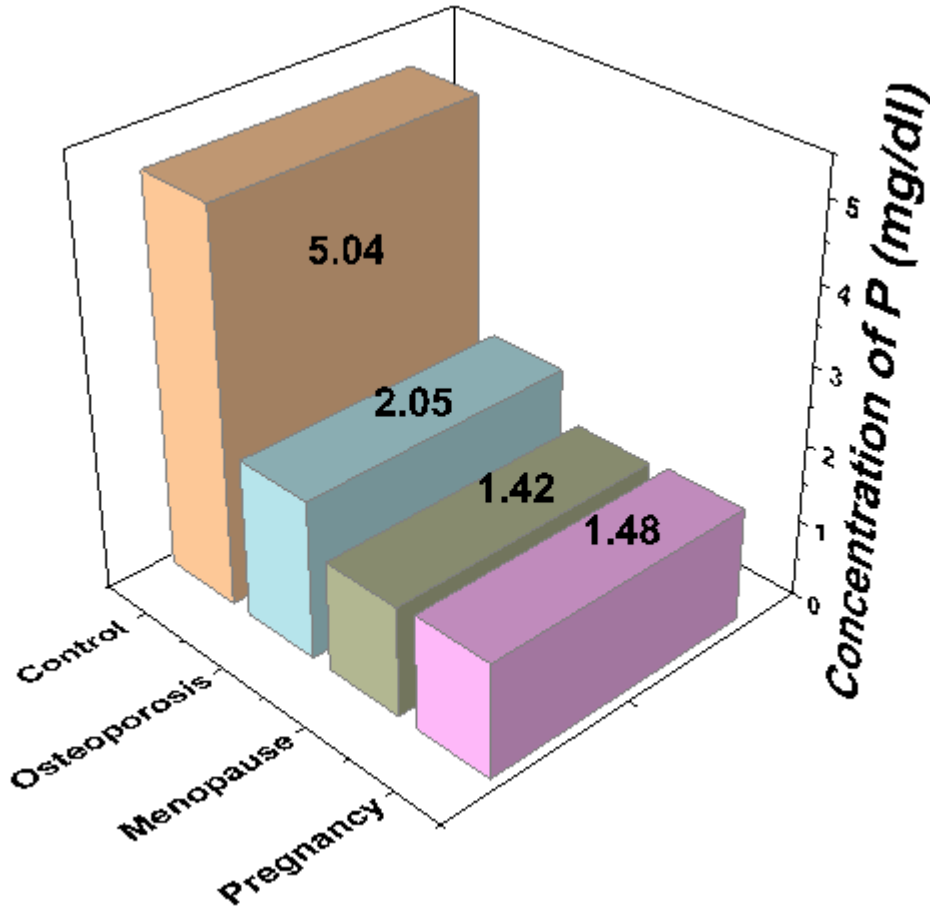
Fig 6. The P concentration in different group study.

The results of the BMI in the study groups of women (Figure 7). The obtained results showed a significant increase in the BMI in the pregnant group, the group of menopausal women, and the group of women with osteoporosis. The values were respectively (26.25±0.12,35.52±0.4, and 28.47±0.18) compared with a control group or healthy group (24.27±0.16) and the results of the current study showed a significant increase in the group of menopausal women compare with the pregnant group and the group of women with osteoporosis. This obtained results are compatible with other reference [34].

Many studies have investigated the relationship between obesity and osteoporosis. However, there is no consensus on this subject, as the skeleton is affected by many different factors such as age, sex, race, genetics, reproduction, calcium intake, BMI, and exercise. Among the most controversial of these factors is the BMI. Many women in menopause suffer from weight gain that may reach more than 2 kilograms per year, according to a study conducted by a team of American researchers, and what makes the matter more complicated is that the weight gained during this period usually accumulates in the form of fat in the abdomen, which represents a greater risk of cardiovascular disease [35]. Increasing BMI has multifactorial effects on bone metabolism, some studies indicated that it is generally accepted that increased body weight promotes bone production and has a protective effect on bone and that adipose tissue is a source

of estrogen in postmenopausal women, while other studies indicated that estrogen deficiency leads to excessive gain and that obese people have growth hormone less than their normal-weight peers. Fat cells produce leptin, which regulates appetite and body weight, and suggests that leptin may reduce bone formation in obese women as a result higher than normal levels and loss of insulin-regulating signals lead to down-regulation of glucose levels leading to an increase in BMI. It has recently been suggested that obesity is associated with low-grade chronic inflammation within adipose tissue and that inflammatory markers stimulate osteoporotic activity to accelerate osteoporosis [36][37].

In pregnant women, the BMI increases gradually with the progression of the months of pregnancy as a result of the physiological changes accompanying it. The natural weight gain is estimated between 10-16 kg. The increase appears in the last trimester of pregnancy. The increase is a result of the weight of the fetus, the weight of the amniotic fluid, the weight of the placenta, the increase in the muscle mass of the uterus, the increase in blood that nourishes the fetus, and organs, fluid retention in the pregnant mother's body, and the increase in stored fats that increase during pregnancy and have a role after birth to provide the body with energy for breastfeeding [38].

The researcher Gkastaris and his colleagues indicated in a study conducted on women that an increase in mineral density was positively associated with an increase in body mass and a decrease in exposure to osteoporotic fractures [39] .
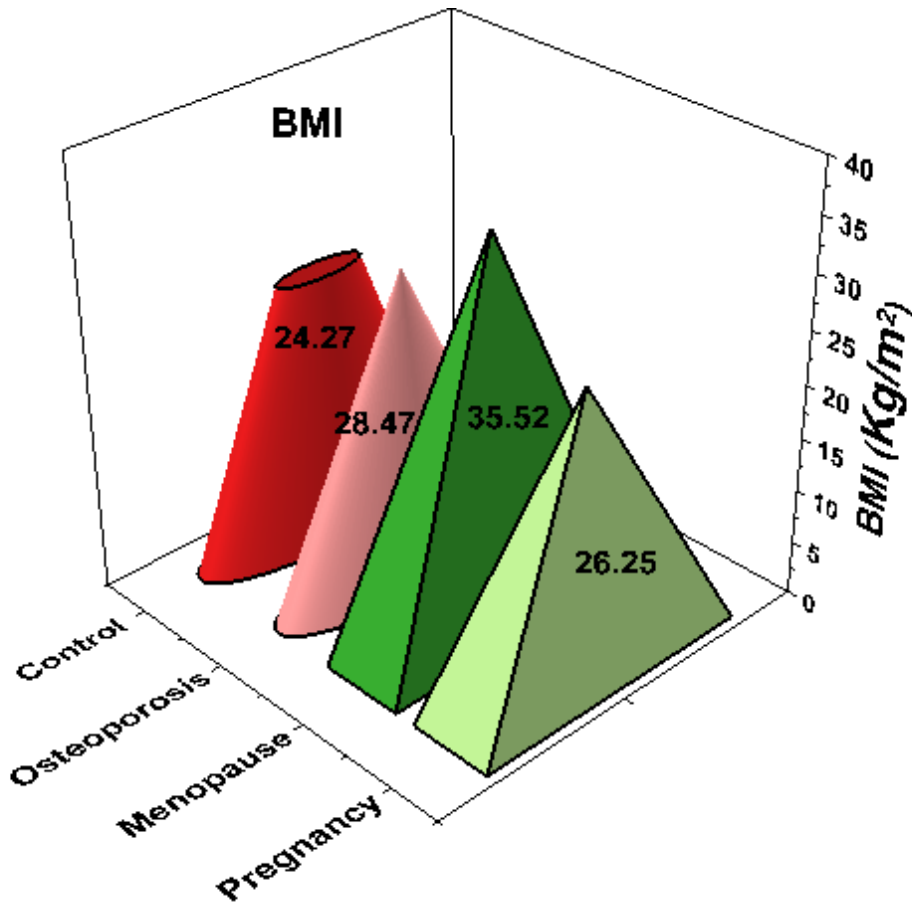

Fig 7. BMI level in different group study.

4. The Correlation Studies

The correlation between current variables was calculated using the STATISCA program (SPP) and the results are shown in Table (1). The high correlations were illustrated in Figure (8.9 and S2).
The direct correlations between some variables were observed, such as Vit -D with P, Hb, and RBCs, also, a good correlation was observed between PTH hormone, Cath-k, and BMI. In addition, between BMI, RBCs, and Hb, HCT. It also showed the existence of negative correlations between some variables such as between P with Cat-k and PTH, Vit -D with PTH, Cat-k, WBCs, BMI and between BMI and Vit-D, E2, RBCs, and P. There is no significant correlation observed between E2 between RBCs, Cat-k and Vit -D.

Table 1. Correlations between variables in different study groups.

	Cat-k	Vit-D	Estradiol	PTH	RBC	HB	HCT	WBC	PLT	P	BMI
Cat-k	1.000000										
Vit-D	-0.971118	1.000000									
Estradiol	-0.253255	0.222464	1.000000								
PTH	0.899223	-0.955480	-0.453183	1.000000							
RBC	-0.863502	0.951414	0.003641	-0.892295	1.000000						
HB	-0.669912	0.691366	-0.542468	-0.466629	0.785855	1.000000					
HCT	-0.170824	0.391621	-0.314745	-0.405465	0.643174	0.475104	1.000000				
WBC	0.563705	-0.548614	0.652621	0.286021	-0.633739	-0.975224	-0.328379	1.000000			
PLT	0.600407	-0.560301	-0.925559	0.720994	-0.334302	0.187731	0.206269	-0.317821	1.000000		
P	-0.984656	0.938716	0.104199	-0.817474	0.843284	0.761489	0.142397	-0.685475	-0.472472	1.000000	
BMI	0.675760	-0.520006	-0.675964	0.536515	-0.231831	-0.018251	0.553083	-0.006964	0.830350	-0.633457	1.000000

The correlation between Vit-D and Cat-K enzyme was illustrated in Figure 8 and showed a negative correlation found to be -0.97.
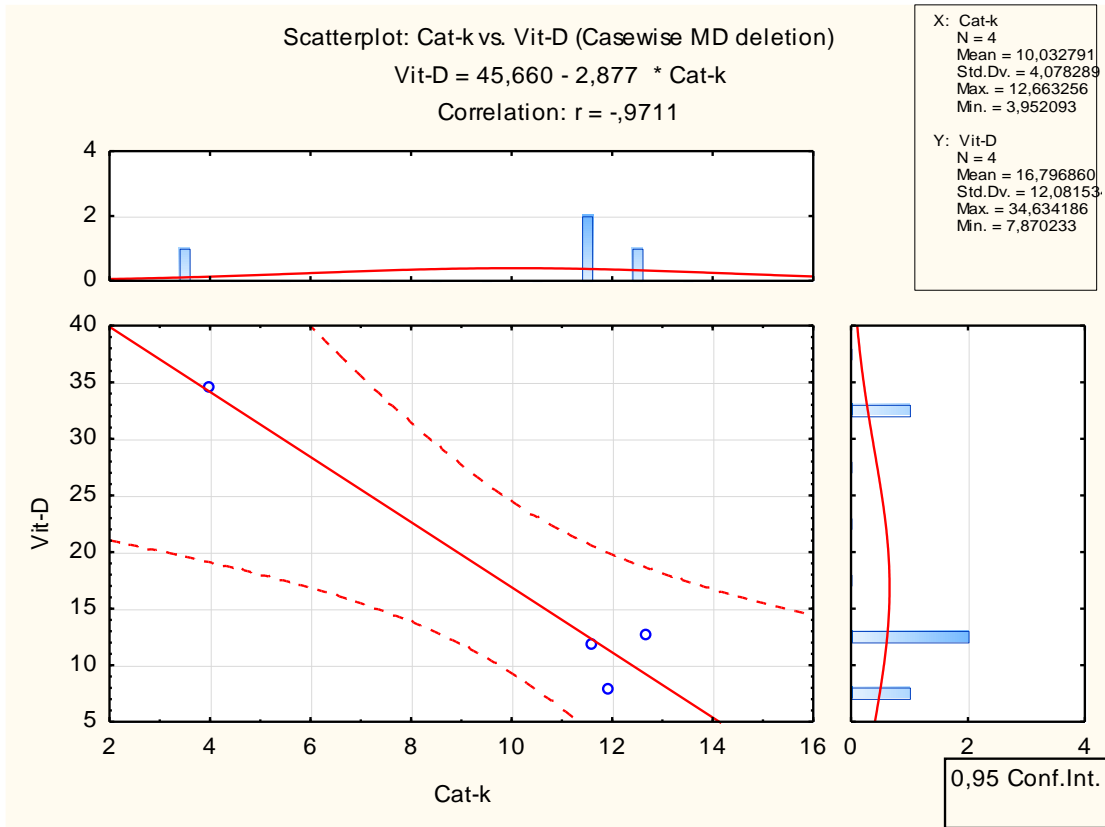
Fig 8. Correlation graphic between Vit-D and Cat-K.

A good correlation was observed between PTH and Cat-k (0.89), which indicated there is a relation between these two parameters. A study by Lotinun et al. showed that deletion of Cat-k in osteocytes increased bone parathyroid hormone-related peptide (PTHrP) and prevented the lactation-induced decrease in serum PTH but amplified the Increased serum 1,25-dyhydroxyvitamin D [1, 25(OH)2D] [40]. Another study confirms that various evidence exists demonstrating that PTH strongly induces Cathepsin-K, a cysteine protease present mainly in the lysosomes of osteoclasts and macrophages that promotes bone and extracellular matrix remodelling. Cathepsin-K levels are altered in various bone disorders, systemic inflammations [41].
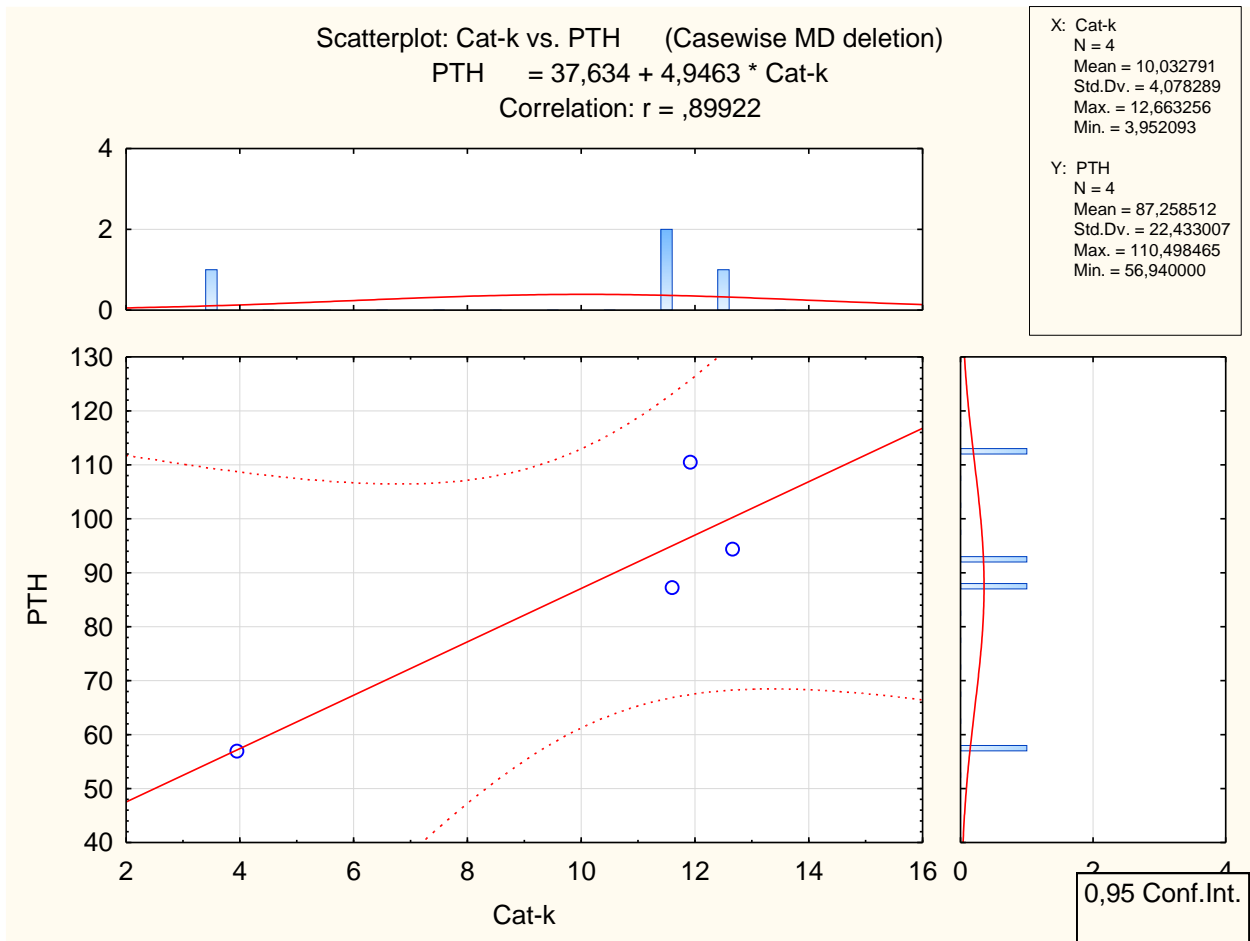
Fig 9. correlation graphic between PTH and Cat-K.

5. Conclusion

According to the obtained results, Cat-k was elevated in the study groups except for the control group, and this indicates the importance of this vital indicator in diagnosing osteoporosis. In addition, a decrease in the concentration of Vit -D in the study groups except for the control, and this indicates the onset of bone diseases, including osteoporosis if treatment is not done. Also, decrease in phosphorus in the study groups except for the control group, indicating a deficiency of mineral elements in the blood serum and the occurrence of bone weakness. High PTH in the study groups except for the control group, indicating a decrease in the calcium component in the blood serum, which causes bone weakness and fragility. Finally, decreased estrogen hormone in postmenopausal women and women with osteoporosis indicates the importance of this hormone in protecting bones from losing the basic mineral elements that makeup bones.

Based on this study, it is recommended to carry out a study on vitamin K and clotting factors released by blood platelets and their relationship with bone health at different ages of pregnant and postmenopausal women.

Thus, to carry out a study on the extent of exposure to the sun and its relationship with the level of vitamin D in women of different ages and its effect on bones and do a study of the relationship between cortisol and melatonin and osteoporosis in different age groups of women and also conduct a study on the relationship between heart disease and

vitamin D and calcium levels and osteoporosis.

Acknowledgement

This article is derived from the master's thesis titled "The Correlation of Cathepsin-k Level with Some Biochemical and Hematological Variables in Women with Osteoporosis, Pregnancy, and Menopausal at Al-Sadr Teaching Hospital in Najaf".

Appendix. Ethics Aproval

Republic Of Iraq
Ministry of Health
Diwaniyah Health Department
Training and Human
Development Centre
No: 2066
Date: 19/03/2023

To Shamiya General Hospital
Regarding Mission Facilitation
Greetings,
In regards to your letter No. 4553 dated on 6/9/2023 concerning the facilitation of the researcher's, Hussein Ali Mashkour, mission to get the ethical approval to conduct the scientific research titled:
The effects of Covid-19 on sugar levels in the blood and the deterioration of kidneys function: a comparative study in the city of Al Diwaniyah, Iraq.
The educational committee at our department center obtained approval to conduct the research in the governorate hospitals affiliated with our department, with an emphasis on full compliance with biosafety instructions and ethical controls, obtaining the approval of research participants before commencing the research, preserving their privacy, and not disclosing data or using samples for purposes other than the aforementioned scientific research.
Informed…with respect
M. D.
Amer Muhssein Hassan Alkhaza'ai
Director General of the Agency

Stamps:
- Pharmacist Asad Hamza Elewah (Director of the technical department - Shamiya General Hospital)
- Dr. Osama Abdalreda Alabadi (Assistant Director General for Technical Affairs)
- Hamed Jamil Naji
- Ministry of Health, Diwaniyah - Shamiya General Hospital- incoming
A copy to:
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Ministry of Health
Diwaniyah Health Department
Training and Human
Development Centre
NO :
Data

جمهورية العراق
وزارة الصحة
دائرة صحة الديوانية
مركز التدريب والتنمية البشرية
العدد : ٢٦٦ ع م
التاريخ : ٩ / ١ / ٢٠٢٣

١٦ ٤٨٩

الى / مستشفى الشامية العام

م / تسهيل مهمة

تحية طيبة ...

اشارة الى كتابكم ذي العدد 4553 في تاريخ في 2023/9/6 بخصوص تسهيل مهمة الباحث (حسين علي مشكور)
للحصول على الموافقة الاخلاقية لأجراء البحث العلمي الموسم :

تأثير كوفيد-19 على مستويات السكر في الدم وتدهور وظئف الكلى: دراسة مقارنة في مدينة الديوانية، العراق

حصلت الموافقة اللجنة العلمية في مركز الدائرتنا على أجراء البحث في مستشفيات المحافظة التابعة لدائرتنا مع
التأكيد على الالتزام التام بتعليمات السلامة الحيوية والضوابط الاخلاقية والحصول على الموافقة المشاركين في البحث
قبل الشروع بالبحث والحفاظ على خصوصيتهم وعدم افشاء البيانات او استخدام العينات لغير اغراض البحث العلمي
المذكور ...

للتفضل بالاطلاع ... مع الاحترام

الطبيب الاختصاص
عامر محسن حسن الخزاعي
مدير عام وكالة
الدكتور

نسخة منه الى :

- مركز التدريب والتنمية البشرية /شعبة ادارة المعرفة والبحوث
- مستشفى الشامية العام
- الاضبارة الشخصية
- البريد والحفظ

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