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Dear Esteemed Readers, Authors, and Colleagues,

I hope this letter finds you in good health and high spirits. It is my distinct pleasure to address you as the Editor-in-Chief of Integrative Omics and Applied Biotechnology (IIOAB) Journal, a multidisciplinary scientific journal that has always placed a profound emphasis on nurturing the involvement of young scientists and championing the significance of an interdisciplinary approach.

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I would like to extend my gratitude to our authors, reviewers, editorial board members, and readers for their unwavering support. Your dedication is what makes IIOAB Journal the thriving scientific community it is today. Together, we will continue to explore the frontiers of knowledge and pioneer new approaches to solving the world's most complex problems.

Thank you for being a part of our journey, and for your commitment to advancing science through the pages of IIOAB Journal.

Yours sincerely,

Vasco Azevedo

Vasco Azevedo, Editor-in-Chief
Integrative Omics and Applied Biotechnology
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ARTICLE

EVALUATION OF IRON AND ZINC FOLIAR AND SOIL APPLICATION ON QUANTITATIVE AND QUALITATIVE CHARACTERISTICS OF TWO SOYBEAN CULTIVARS

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ABSTRACT

In order to investigate the effects of foliar and soil application of iron and zinc on quantitative and qualitative yield of two soybean cultivars, a field experiment was laid out in factorial arrangement based on completely randomized block design with three replications at Rice Research Institute of Iran (Rasht) in 2014. Treatments include iron foliar application, iron soil application, zinc foliar application, zinc soil application, iron and zinc foliar application, zinc soil application + iron foliar application, iron soil application + zinc foliar application, iron and zinc soil application, iron and zinc foliar and soil application and control was used. Result of showed that iron foliar application + zinc soil application increased stem height and biological yield. Highest rate of seed number per plant,, seed yield, harvest index and seed protein content was observed in zinc soil application treatment (152.4, 16.53 g, 8285.88 kg ha^{-1}, 43.01% and 65.25% respectively). Also results showed that oil and iron content of seed was affected by iron soil application and zinc soil + foliar application. The results of this experiments showed that the consumption of iron and zinc can be improved physiological characteristics, yield and grain quality of soybean.

KEY WORDS
Fe Secostrain, Microelement, Oil, Seed protein, Zinc sulfate.

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INTRODUCTION

Soybean (*Glycine max*) is a common legume plant and cultivated for more than 3000 years in Southeastern Asia. Soybean plants first in the world as edible oil and occupies important place in the economy. Climatic and edaphic factors severely affect its production; It has been also well reported that deficiency of micronutrients such as Fe, Mn and Zn affect the soybean production [1]. Furthermore, various researcher reported that the application of essential micronutrients such as zinc, iron and magnesium improve the yield and yield components of crops [2, 3]. Plant sufficient nutrition have an important role in raising level of plants tolerance against a variety of environmental stresses and in this regard, iron and zinc are the most important essential micronutrients in plant nutrition [4]. Micronutrients also play key roles in the release of carbon dioxide, and in optimizing the function of vitamin A and the immune system [5]. Zinc plays an important role as a metal component of enzymes (alcohol dehydrogenase, superoxide dismutase, carbonic anhydrase and RNA polymerase) or as a functional, structural, or regulator cofactor of a large number of enzymes [6]. Experimental result of [7] also showed that foliar application of micronutrients increased the soybean yield, quality, resistance to pests and diseases and drought stress. They reported that although the need of plants to micronutrients is very little but these nutrients play an important role in growth and development of plants. So that the micronutrients such as iron, copper, boron, zinc and manganese have many contributions in cell wall formation and plant resistance to pests and diseases and environmental stresses.

Normally fertilization carried out in soil but in this condition very less amount of nutrient reached to the plant system and remaining amount waste through leaching in soil, it also cause land and water pollution. Foliar fertilization is better option to avoid leaching and in this quick translocation of nutrients carried out in different parts of the plant system [8].

The aim of this study was to evaluate the effects of foliar and soil application of iron and zinc, individually and in combination on yield and yield components and grain quality traits of two soybean cultivars.

MATERIALS AND METHODS

In order to investigate the effects of foliar and soil application of iron and zinc either individually or in combination on yield, yield components and quantitative traits of two soybean cultivars (Williams and Sahar), a field experiment was carry out at rice research institute of Iran, Guilan (37°, 16´ N, 51°, 3´ E and 7 m above sea level) in 2014. The experiment was carried out in factorial arrangement based on completely randomized block design with three replications. Treatments include iron foliar application, iron soil application, zinc foliar application, zinc soil application, iron and zinc foliar application, zinc soil application + iron foliar application, iron soil application + zinc foliar application, iron and zinc soil application, iron and zinc foliar and soil application and control were used.

Table 1: Physical and chemical soil properties

Soil texture	Fe (mg kg^{-1})	P (mg kg^{-1})	(%) N	K (mg kg^{-1})	Zn (mg kg^{-1})	Ca (mg kg^{-1})	Ec (ds m^{-1})
Clay loam	2.2	14	0.03	220	0.22	10.2	2.6

The experimental field received 100 kg ha^{-1} P_2O_5 (in the form of triple superphosphate) and K_2O (in the form of potassium sulfate) before planting. Nitrogen at rate of 100 kg ha^{-1} (in the form of urea) was applied in two stages: before planting and fourth interned stages. Seed were planted on 5 June 2014 in 50 cm row space, 5 cm plant space within row (density of 40 plant m^{-2}) in 3×5 m plots.

Different treatments of micronutrient soil application which were including: 20 kg ha^{-1} iron from secostrine and 30 kg ha^{-1} from zinc sulphate were distributed in plots and mixed with surface soil before seed sowing. Micronutrient foliar application was done at three times, one time when plants had two nodes, second time in 50% flowering and another in 50% podding stage. The iron and zinc were sprayed on plants with concentrate of 2 parts per thousand and 3 part per thousand, respectively. In control treatments plants were sprayed by water. Description of all treatments is shown in [Table 2].

Table 2: Different treatments of micronutrient application

F_1	Iron (foliar application)	2 parts per thousand
F_2	Iron (soil application)	20 kg ha^{-1} iron from secostrine
F_3	Zinc (foliar application)	3 parts per thousand
F_4	Zinc (soil application)	30 kg ha^{-1} zinc sulphate
F_5	Iron + Zinc (foliar application)	2 parts per thousand + 3 parts per thousand
F_6	Zinc (soil application)+ Iron (foliar application)	30 kg ha^{-1} zinc sulphate+2 parts per thousand
F_7	Iron (soil application)+ Zinc (foliar application)	20 kg ha^{-1} iron from secostrine+3 parts per thousand
F_8	Iron + Zinc (soil application)	20 kg ha^{-1} iron from secostrine + 30 kg ha^{-1} zinc sulphate
F_9	Iron + Zinc (soil and foliar application)	20 kg ha^{-1} iron from secostrine + 30 kg ha^{-1} zinc sulphate + 2 parts per thousand + 3 parts per thousand
F_{10}	Control	Water

At harvest, ten plants were taken at random from the central ridge to estimate: plant height, number of seed/plant, seed yield, biological yield and harvest index, straw and seed yields were determined from the three central ridges. Moreover, samples of soybean seeds were oven dried at 60-70°C for 48 hours ground to pass through a 0.5 mm sieve and sub samples of 0.2 g portions were wet digested using a mixture of sulphuric (H_2SO_4) and perchloric (HClO) 4acids. The digest was analyzed for N. Total nitrogen percentage (N %) in seeds was determined to the modified micro Kjeldahl method. Crude protein content in seeds was estimated by multiplying nitrogen percentage X 6.25.

Total oil content of soybean seeds was determined by using the soxhlet device; the pure seeds of each treatment were dried and weighted before insert into the device. The chloroform was used as solvent, it is a popular solvent seed oil extraction, particularly for lipids of intermediate polarity and when mixed with methanol it becomes a general extraction solvent. So the dried and powdered seed samples were inserted into the soxhlet device and the extraction was completed by evaporating the solvent.
After that, for determine of Fe and Zn content of seeds, the samples were washed by distilled water and dried in oven at 70°C during 48 h. Total Fe and Zn content were determined through atomic absorption method (Elmer Perkin 3030). Data analysis performed by using Statistical Analysis System (SAS) and the mean comparisons were evaluated based on Least Significant Differences (LSD).

RESULTS AND DISCUSSION

Seed Yield: The results showed that, the interaction effect of cultivar and treatment on the grain yield was significant [Data not shown]. Mean comparison showed that the maximum amount of seed yield was observed in Sahar × zn soil application treatment (F_4) (8774.8 kg ha^{-1}). There was no significant difference between F_4 and F_3. Minimum amount of seed yield was observed in Williams × Iron + zinc soil and foliar application (4107.1 kg ha^{-1}) [Table 3]. The interaction of various micro-nutrients (Fe, Zn) showed a positive and significant response to growth and yield parameters of soybean. Heitholt *et al* [9] reported that seed yield of soybean increased while Cu, Mn, Zn, and Fe applied individually.

Rose *et al* [10] reported that two time's foliar applications of zinc (40 kg ha^{-1}) increased soybean grain yield from 58 to 208 percent. Considering the results of this study 25 kg ha^{-1} Fe and 40 kg ha^{-1} Zn produced the highest seed yield and biomass. In contrast, Kobraee *et al* [11] also claimed that zinc and iron application at the same time could be lead to higher dry matter and seed yield as compared to using them separately.

Shiraiwa *et al* [12] declared that pod number and seed number are two important factors which affect soybean seed yield. Variation in dry matter production in seed filling period is a prime factor for different seed yield in soybean genotypes. In soybean, as a result of increasing the ratio of source-sink during flowering stage, seed yield was increased by the seed number enhancement [13].

One of the most important factors which are determiner in soybean seed yield is pod number per plant. The rate of pod set in soybean raised with an enhancement in source vigor at the time at which sink/source ratio was altered by flower thinning and defoliation. Furthermore, the ratio of dry matter enhancement in soybean seeds to its shoot is a crucial factor which affects the rate of podding in soybean [13].

In proceed to the previous studies [14] all methods of Zn application for plants significantly increased grain yield. Micronutrients increases photosynthesis rate and improves leaf area duration thus seed yield will be increased. Zinc plays important role in tryptophan biosynthesis, later is precursor of auxine also zinc is founded in phosphoenolpyruvate carboxylase structure. Another element that is iron is necessary to chlorophyll synthesis and its critical element in electron transport chain in photo systems. Iron deficiency leads to many disorders in chloroplasts. Ferredoxin is an important iron-containing protein involved in electron-transfer.

Biological Yield: The results showed that, the interaction of cultivar and fertilizer treatment on biological yield was significant [Data not shown]. Mean comparison showed that the maximum amount of biological yield was observed in

Sahar × zinc (soil application) + Iron (foliar application) (F_6) (25785.9 kg ha^{-1}). There was no significant difference between F_6 and F_4 (24880.7 kg ha^{-1}). Minimum amount of biological yield was observed in Williams× iron + zinc soil and foliar application (13674.3 kg ha^{-1}) [Table 3]. Such effects of micronutrients (Zn) application might be due to their critical role in crop growth, involving in photosynthesis processes, respiration and other biochemical and physiological activates and thus their importance in achieving higher yields [15]. Also, Cakmak [16] reported that zinc plays an important role in the biomass production. Zn and Fe applications separately have better effect than their combination. Decrease of biological yield in F_9 (Fe+ Zn. soil and foliar application) can be attributed to antagonistic effect among Fe and Zn in their combination.

Iron plays essential roles in the metabolism of chlorophylls. External application of Fe increased photosynthesis, net assimilation and relative growth in seawater-stressed rice [17]. This is especially true for soils of high pH where equilibrium conditions favour the oxida tion of plant-available Fe^{+2} to unavailable Fe^{+3}. Plant yield on many soils is, therefore, limited by poor Fe availability, rather than a low Fe content in the soil. Also Fe leaching is the main pathway for Fe loss in coarse-textured soil with high pH, while excessive Fe uptake was the main pathway for Fe loss in clay-textured and acid soil [4].

Table 3: The mean comparison of the interaction of cultivars and treatments on measured traits in experiment

Cultivar	treatments	Mean Squares				
		Seed yield (kg ha^{-1})	Biological yield (kg ha^{-1})	Harvest index (%)	Plant height (cm)	Seed/plant
	F_1	6646.6 bcdef	14684.8 h	43.80 bc	143.90 b	18.96 gh
	F_2	5866.9 efg	14685.4 h	39.91 de	143.20 b	116.08 hij
	F_3	7519.4 abcdef	18351.3 d	42.07 cd	144.36 b	105.13 k
	F_4	8263.5 abc	17868.3 ef	46.46 ab	13740 bc	147.40 bc
	F_5	6637.3 bcdef	17200.8 fg	39.48 de	138.16 bc	108.73 jk
Williams	F_6	8074.9 abcd	17971.8 ef	47.88 a	168.73 a	133.30 def
	F_7	5459.5 fg	16181.6 g	33.86 f	140.30 bc	101.60 k
	F_8	8043.6 abcd	16997.9 fg	45.24 abc	131.43 cd	140.26 cde
	F_9	4107.1 g	19268.0 d	26.30 i	126.90 de	86.73 l
	F_{10}	6079.6 def	13674.3 h	41.59 cde	136.06 bcd	126.13 fg
	F_1	8774.8 a	25785.9 a	34.46 f	130.73 cd	131.13 ef
	F_2	7618.8 abcde	18386.9 de	41.66 cde	101.80 ij	141.50 cd
	F_3	6330.8 cdef	23492.9 b	26.95 hi	110.80 ghi	119.00 ghi
	F_4	8251.6 abc	21561.7 e	38.38 de	117.80 efgh	157.40 a

Sahar	F_5	6304.4 cdef	19352.0 d	32.23 fg	99.40 j	110.13 ij
	F_6	6640.9 bcdef	17505.1 ef	38.15 e	108.60 hi	146.76 bc
	F_7	5651.3 efg	18331.2 de	30.84 fg	119.80 efg	154.83 ab
	F_8	8639.3 ab	24880.7 a	34.26 f	115.93 fgh	148.93 abc
	F_9	6258.6 cdef	17320.8 ef	30.00 gh	126.90 de	152.86 ab
	F_{10}	6050.4 def	21405.7 c	39.32 ed	120.85 ef	126.29 fg

In each column, the means that have at least the same letters are not significantly different by L.S. Means test.

Harvest Index: Mean comparison showed that the highest harvest index was recorded in Williams × zinc soil application (F_4) (47.88%). Lowest harvest index also recorded in Williams× iron + zinc soil and foliar application (26.3%) [Table 3]. Bameri *et al* [18] demonstrated that foliar application with micronutrient either separately or in mixture significantly increased harvest index.

Whereas, F_4 treatment produced maximum grain and biological yield, so increase harvest index in this treatment is absolutely. The increase in the studied characters due to micronutrients may be attributed to its influences in enhancing the photosynthesis process and translocation of photosynthetic products to the seed as a result of increase enzymatic activity and other biological activities.

Plant Height: Results showed that the highest plant height was recorded in Williams × zinc soil application + iron foliar application (F_6) (168.73 cm) and lowest plant height recorded in Sahar × iron + zinc soil and foliar application (99.40 cm) [Table 3]. Micronutrients have a structural role in chlorophyll. These elements can be easily sprayed on leaf, thus leaves chlorophyll concentration increased by micronutrient foliar application, which in turn, lead to an increase in plant height and yield. Also zinc, increased plant height via increasing internodes distances. Plant height was significantly affected by foliar application of Fe, Mn and Zn individually and combined [18].

Seed Number of Plant: Maximum amount of seed number per plant was observed in Sahar × zinc soil application (F_4) (157.4). There was no significant difference between F_4 and F_3, F_2, F_1. Minimum amount of seed number per plant was observed in Williams× iron + zinc soil and foliar application (86.73) [Table 3]. Maximum 100 grain weight was found in Williams × zn soil application treatment (F_4) (20.17 g). There was no significant difference between F_4 and F_3. Minimum 100-seed weight was found in Sahar× Iron + Zinc soil and foliar application (10.87 g) [Table 3].

Number of pods per plant in soybean was enhanced by zinc application. Zinc application enhanced soybean yield by influencing the number of seeds per plant and seed weight. Zeidan *et al* [15] also reported that yield components in lentil are enhanced by foliar application of micronutrients. Due to the enzymatic activity enhancement, microelements effectively increased photosynthesis and translocation of assimilates to the seed. Previous researches showed that highest pods per plant was produced by foliar spraying at flowering and poding stage and increase of number of pods per plant due to foliar application could be attributed to significant effect of microelements on reproductive organs, such as stamens and pollens. These authors revealed that since soybean is a self-pollinated crop, stamen activity enhances the number of flowers that can fertile well and as a result, larger number of pods per plant will be produced [19]. Probably zinc may increase the amount of carbon hydrates and led to increase rates of seed.

Seed Protein Content: The results of this study showed that there were significant interaction effects of cultivar and treatment on seed protein content [Data not shown]. The lowest seed protein content (34 %) was recorded in Sahar × iron + zinc soil and foliar application treatment (38.84%) while the highest seed protein content (67.83%) was noted in Williams × iron foliar application + zinc soil application (F_6) [Table 4].
Fe+Zn foliar application compared to the control treatment could increase the grain protein content about 16% [Table 4]. Baybordy and Mamedov [4] explained that Iron and zinc are two important elements in enzymes structure involved in amino acid biosynthesis and because amino acids are the base of protein synthesis, protein content increases in the case of using these micronutrients. The results obtained by Thalooth *et al* [20] showed that using of zinc sulfate increases grain protein content of mungbean. In addition, iron is involved in the metabolism of nitrogen and increases leaf area and has a direct impact on the process of protein production. So it can be expected that iron foliar application, increased the plant protein production.

Seed Oil Content: The highest oil percentage was obtained from Sahar× iron soil application (12.22%).The lowest oil percentage was obtained from Sahar× iron + zinc soil and foliar application (7.7%) [Table 4]. It seems that, soil application of micronutrients is more benefit to oil biosynthesis. Singh and Sinha [21] reported the decrease in oil concentration may be due to oxidation of some polyunsaturated fatty acids. In general, there was not significant different between micronutrient application method.

Seed Iron Content: Mean comparisons showed that the interaction between Sahar × iron soil application could be increasing the concentration of iron in the grain about 9% compared to the control treatment and

32% compared to the iron foliar application treatment in Williams cultivar, that showed minimum seed iron content (72.51%) [Table 4]. Baybordy and Mamedov [4] by foliar application with iron in canola increased the amount of iron in grain that confirmed the results of this experiment.

The application of Fe through soil as well as foliar application caused a marked increase in the total content of Fe in the soybean plants. Whereas in foliar application method iron absorption is faster and easier that soil application the highest iron content was observed in these treatments. In soil application due to organic matters banding with chemical fertilizers that have high ability to absorb and hold nutrients, and positioning these substances near hairy roots, results in better availability to plant and thus causing in higher iron content. Studying previous researches show that best results achieved in using iron sulphate [22]. And may be the use of zinc sulphate causes better absorption in iron. Iron deficiency leads to chlorophyll degradation and chlorosis. It's reported that, iron is an essential element in protein synthesis and iron deficit decreases plant growth. Also, iron is involved electron transport in photosystems. Already decrease of chlorophyll content due to iron deficit was reported.The results of this study indicate that due to high humidity in the weather conditions of Gilan province, iron soil application can be more effective than Iron foliar application to increase the concentration of this element in grain. Because iron would be oxide in the air and the plants would not be able to absorb it.

Seed Zinc Content: The highest zinc content was obtained from Williams × zinc soil application (60.42 mg kg^{-1}), there was no significant difference between zinc soil application and zinc foliar application treatment (59.27 $mg.kg^{-1}$). The lowest zinc content was obtained from Sahar × iron soil application (33.54 mg kg^{-1}) [Table 4]. Grain micronutrients concentration depends on their uptake by root during the seed development stage and remobilization from plant tissues to grain through phloem. Amount of remobilization from this way has largely depended on each element moves in the phloem and zinc has

good remobilization from leaves to the grain. Kazemi Poshtmasari *et al* [23] also increased concentration of this element in bean grain by using of zinc foliar application, which confirmed the results of this experiment. Zinc is essential element in enzymatic system such as superoxide dismutase enzyme. Zinc plays important role in auxine and protein synthesis and it is essential for seed setting. Abdili *et al* [24] observed that consumption of sulfate zinc in 40 kg per hectare increase grain yield of soybean by 19%, zinc content of grain by15%, the concentration of the plant by 46% and total uptake of Zn by grain 37% rather than control treatment.

Table 4: The mean comparison of the interaction of cultivars and treatments on measured traits in experiment

Cultivar	Treatments	Mean Squares			
		Protein content (%)	Oil content (%)	Fe content (mg kg^{-1})	Zn content (mg kg^{-1})
Williams	F_1	54.80 de	11.54 abc	87.49 j	36.76 j
	F_2	53.08 e	9.40 ef	88.44 hi	38.40 i
	F_3	54.43 de	11.34 bc	72.51 o	58.50 b
	F_4	65.92 a	10.58 d	90.26 gh	44.71 ef
	F_5	56.45 de	10.62 d	74.44 n	38.80 i
	F_6	46.52 f	9.78 e	79.31 l	41.40 h
	F_7	55.49 de	8.44 g	73.57 no	60.42 a
	F_8	54.93 de	11.06 cd	79.79 l	45.90 e
	F_9	67.83 a	8.45 g	93.60 de	53.32 c
	F_{10}	34.89 h	8.90 fg	94.35 d	44.17 fg
Sahar	F_1	47.99 f	10.62 d	92.19 ef	33.54 l
	F_2	62.23 abc	9.18 efg	106.22 a	35.50 jk
	F_3	38.84 gh	12.22 a	98.27 c	53.51 c
	F_4	43.16 fg	7.72 h	77.46 m	34.43 k
	F_5	54.03 e	11.84 ab	90.23 gh	47.61 d
	F_6	59.81 bcd	9.36 ef	89.38 hi	34.73 kl

	F_7	63.33 abc	8.98 fg	101.15 b	42.77 gh
	F_8	58.52 cde	9.41 ef	91.34 fg	39.68 i
	F_9	62.67 abc	7.70 h	83.42 k	59.27 ab
	F_{10}	44.21 fg	8.82 fg	97.66 c	34.25 k

In each column, the means that have at least the same letters are not significantly different by L.S. Means test.

CONCLUSION

Uses of micro nutritious elements especially zinc and iron alone or combination had positive effect on yield and yield components. Iron and zinc uptake are controlled by the two major factors, availability of these elements in the soil and the ability of plants to acquire them. Application methods of micronutrients are very important to attain the best absorption. Sometimes response of the plants is different to application methods of fertilizers, for example in calcareous soil Fe and Zn are not available for plants, in this times, foliar application is a useful method for nourish of the plants. The results of this study demonstrated that, Fe and Zn had positive effect on yield and quality of soybean oil, protein, zinc and content. Overall, when plants like soybean are not supplied with an optimum amount of Fe and Mo due to environmental limitation, growth inhibition and physiological changes will be appear more quickly, depending on the strength and duration of the imposed stress. Negative response to two combination (Fe+Zn) foliar application on quantitative and qualitative characteristics of soybean may be attributed to micronutrient uptake problems and antagonistic effect among Fe and Zn in their combination.

CONFLICT OF INTEREST

There is no conflict of interest.

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None

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ARTICLE

STUDYING THE LEVEL OF MICROBIAL INFECTION OF MOBILE PHONES AMONG NURSES WORKING IN THE INTENSIVE CARE UNITS OF HOSPITALS

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ABSTRACT

Background:*The problem of hospital infections is a great common problem in all hospitals and health centers. As using mobile phones becomes more and more common among all people including the health workers, there is a growing concern that this tool can act as a source to distribute hospital microorganisms throughout the society. The present research aims to study the level of microbial infection observed in the mobile phones of nurses working in the ICU of Besat Hospital in Tehran, Iran in February of 2016.* ***Method:*** *In this study 25 nurses working in the ICU of Besat Hospital were chosen by random selection Demographic information, attitudes, awareness, type of mobile phone, and frequency of cleaning the cellphone per a day were collected in certain questionnaires. In order to assess the microbial infection of mobile phones, wet sterile swabs were used for sampling and the process of cultivation was carried out in the medium containing nutrients.* ***Results:*** *In this study about 65.3% of the mobile phones devices has been found infected. The following bacteria were observed: Staphylococcus epidermidis (26.7%), Staphylococcus aureus (20%), Non-albicans candida (16.7%), Bacillus SP (13.3%), Micrococcus SP (10%), Non-hemolytic streptococcus and Enterococcus (6.7% each) and Acinetobacter and Klebsiella (3.3% each).* ***Conclusion:*** *Mobile phones can act as the potential transporters of hospital infections and the level of infection is significantly higher in smart phones (than non-smart ones) owned by males (compared to their female peers). Thus, limiting the use of cellphone devices is an option which can be considered in the ICU of hospitals. Keeping in mind the significant influence of cleaning these phones in reducing the bacterial infections, regular dis-infection of cellphones and observing the principles of hygiene in hospitals is a crucial point.*

KEY WORDS
Mobile Phones, Nurses, ICU, Microbial Infections, Hospital Infections.

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INTRODUCTION

Hospital infections are increasing every day and it may result in a higher death rate. As many as 25% of the patients hospitalized in the hospitals in developed countries experience this issue [1]. For US hospitals, an annual rate of 1.7 million cases of patients with hospital infections are reported while 100 thousand of them will pass away [2]. The infectious agents of hospital infections may spread through hands of hospital personnel, thermometers, stethoscopes, and even the toys used in the pediatric intensive care unit in the whole hospital [1].

The first global determination to use mobile phones to establish better communication was made in Europe in 1982. Nowadays, mobile phones have became into a necessary tool for social and professional life. Although they may kept in pockets or purses, they are often held in the hand of users and are in direct contact with their faces [3]. Now days mobile phones may use everywhere including dinner tables, kitchens, restaurants, clubs, and even bath rooms. These factors and the heat generated by these phones results in the significant growth of bacteria on the surface of the devices [2].

Using mobile phone is often observed in hospital halls, labs or ICU where patients with serious problems are kept [1]. Widespread use of mobile phones among the medical staff of hospitals is a contradiction. The major question here is how we can use mobile phones and reduce its harms. For example in cases of emergency, surgeons can use their mobile phones to consult with their professors or colleagues and ask technicians for help when proper function of operation room devices has fail but these mobile phones, may cause infections in patients [4].

In a research conducted by Ulger et al (2009), as many as 94.5% of mobile phones were infected with various types of bacteria. 31.3% of these phones were infected with gram negative bacteria and 39.5% of the bacteria observed in the hands of their users were resistant against Ceftazidime. Also 52% of the mobile phones were infected with Staphylococcus aureus and the hands of the users in this group were also resistant against Methicillin (MRSA) in 37.7% of the cases. Re-searches have found similar microbes on the people's hands and cellphones [4]. Another research conducted by Badr et al (2012) showed that hand contamination of hospital staff following using mobile phones had increased 93.7% [3]. In another research conducted by Singh et al (2012) no microorganisms had developed in the second cultivation obtained from mobile phones after they had been cleaned using an alcoholic pad [2].

Concerning the importance of hospital staff awareness of pathogens and observing the rules of hygiene and due to lack of a comprehensive research on the potential role of mobile phones in spreading pathogens in our country, the present research aims to study the infection level of mobile phones used by

nurses working in ICU and their role in spreading bacterial infection in Besat Hospital of Tehran in February of 2016.

MATERIALS AND METHODS

In this cross-sectional, descriptive-analytical research that carried out in 2016. The nurses working in the ICU of Besat Hospital of Tehran in February of 2016 has been considered as research population. Considering the formula used to calculate the sample volume for descriptive researches and keeping in mind the initial error level of our research (0.05), 0.95 possibility of mobile phones bacterial contamination (according to the previous researches [3]) and accuracy of researches set to a 10% possibility of mobile phones bacterial infections, at least 20 people were needed for the research. This number was further increased to 25 through convenient sampling method in order to enhance the accuracy.

Demographic information, attitudes, awareness, type of mobile phone, and frequency of cleaning the cellphone per day were collected in certain questionnaires. Samples were taken from mobile phones of nurses using sterilized swab. Another sample was taken from the phones after they had been cleaned with alcohol swabs. Sterilized swabs, test tubes containing nutrient broth medium, plates containing containing blood agar medium, and Macconkey agar were used for sampling. Sterilized swab was drenched in the tube containing liquid medium. After these swabs were drenched with the liquid inside the test tube, they were removed and contacted with a specific area of mobile phones (5 square cm) and then put inside the test tube containing nutrient broth medium. Then the test tubes were incubated for 24 hours with a temperature of 37 °C in lab. Using swabs, the contents of these test tubes were inoculated to solid medium plates (Macconkey and blood agar). After 24 hours, the number of colonies on mediums was determined, states of being gram positive or negative and accurate diagnosis of type and species were examined. It is clear that controlled experiments of media and sampling the surfaces were carried out simultaneously following dis-infection.

Chi-square and Fisher's exact test were used to determine the correlation between qualitative variables, while T test was used to compare the averages between the two groups. The level of significance was set to 0.05 in all cases.

RESULTS

The results of this research are presented in [Table 1]. The average age of the nurses participating in this research was 32.1 ± 2.7 years. Also 32% of the participants were male while and 68% were female and 72% of the nurses owned smart phones while 28% used non-smart phones (cellphones with no smart operating system). All nurses were aware of the possibility of transporting microbial agents through mobile phones and also of removing risk factors by cleaning the mobile phone, so. 60% of the nurses used to clean their phones more than once a day, while 24% of them cleaned their mobile phones only once a day. And beside them 16% of them never cleaned their mobile phones. Comparing the male and female nurses in terms of the frequency of cleaning their mobile phones every day showed that the frequency of cleaning among the female nurses was significantly more than what was observed among their male colleagues ($P = 0.026$).

The frequency of microbial contamination in all mobile nurses' phones was 64% before cleaning, while this frequency was reduced to 8% following cleaning the phone and this difference was significant ($P < 0.001$). The frequency of microbial contamination observed in the mobile phones owned by male nurses was significantly more than what was observed in female nurses (70.6% for males and 30.8% for females, $P = 0.030$). A higher frequency of microbial contamination was observed in smart phones than what was observed non-smart ones (66.7% for smart phones and 22.2% for their non-smart counterparts, $P = 0.046$).

Table 1: Results of the research

Variables		Frequency (percentage)
Gender	Male	8 (32%)
	Female	17 (68%)
Type of phone	Smart	18 (72%)
	Non-smart	7 (28%)
State of awareness	Aware	30 (100%)
	Not aware	0 (0%)
Attitude	Favorable	30 (100%)
	Unfavorable	0 (0%)
How often they clean their phones every day		
	Never	4 (16%)
	Once	6 (24%)
	Twice	10 (40%)
	Thrice	5 (20%)
Microbial contamination	Positive	16 (46%)
	Negative	9 (36%)
	Staphylococcus epidermidis	8 (26.7%)

Microorganisms observed on the surface of mobile phones	Staphylococcus aureus	6 (20%)
	Non-albicans candida	5 (16.7%)
	Micrococcus SP	3 (10%)
	Non-hemolytic streptococci	2 (6.7%)
	Enterococcus	2 (6.7%)
	Klebsiella	1 (3.3%)

8 types of bacteria were found n the samples made from 25 cellphones before cleaning them: Staphylococcus epidermidis in 8 phones (26.7%), S. aureus in 6 phones (20%), non-albicans candida in 5 phones (16.7%), Bacillus SP in 4 phones (13.3%), Micrococcus SP in 3 phones (10%), non-hemolytic streptococcus and Enterococcus in 2 phones (6.7% each) and finally Acinetobacter and Klebsiella in 1 phone (3.3% each). It is necessary to say that the result of cultivation after cleaning the phones was positive in only 2 cases where Staphylococcus epidermidis and Micrococcus SP (each in only one phone) were observed. Both of these phones were contaminated with these microorganisms before cleaning.

DISCUSSION

Hospital infection is a growing problem in many hospitals and health centers [5-7]. Hands, tools, mobile phones or other non-animate things in hospitals used by therapeutic staff can act as vectors transporting microorganisms in hospitals [2, 8-10]. Unlike stationary phones, mobile phones in these centers are used in the close proximity of patients who are vulnerable to infections [11, 12]. The present research seeks to study the frequency bacterial contamination in the mobile phones of nurses working in the ICU of Besat Hospital in February of 2016 in Tehran, Iran.

As many as 25 mobile phones belonging to 25 male and female nurses were studied in terms of their contamination with bacteria and the results indicated microbial contaminations in 16 cases (64%).

Studies conducted throughout the world are indicative of prevalence of microbial contaminations in the mobile phones of the therapeutic staff of hospitals. A research conducted by Karabay et al [1] in Turkey showed that as many as 91% of the mobile phones owned by therapeutic staff were contaminated by bacterial factors. In a study by Tagoe et al [13] in Ghana has been reported that 47% of the mobile phones owned by medical nurses are contaminated with bacteria. The research by Sepehri et al [14] in Kerman showed that 32% of the mobile phones of therapeutic staff were contaminated with bacteria.

As it is seen, the prevalence of microbial contamination in the mobile phones owned by therapeutic staff in some cases is more than what was observed in our research, while this frequency is less in some other cases.

Totally 8 types of bacteria were observed in the 25 mobile phones studied in this research. The most common one was S. epidermidis observed in 26.7% of cases (8 phones).

The prevalence of Staphylococcus in hospital infections throughout the world is on the rise and statistical analysis in most countries has shown S. epidermidis the most common cause of blood and urinary tract infections [15, 16].

The next prevalent microorganism was S. aureus observed in 6 cases (20%). Among the various species of Staphylococcus, S. aureus has been diagnosed as one of the most important pathogenic factors and one of the main causes of hospital infections [17]. The third microorganism observed on the mobile phones of nurses was Non-albicans candida observed in five phones (16.7%).

Although albicans candida as one of the most common causes of Candidiasis is very important that, recent epidemiological researches have proven that non-albicans candida will gradually replace albicans candida in causing the diseases [18-20]. The frequency of Candidaemia as a result of non-albicans candida among hospitalized patients has increased more than 500% compared to 1980s [2]).

Most species of this bacteria are associated by the diseases caused by foods which can result in severe or even lethal infections. Due to formation of endospore, these bacteria are resistant against to certain types of disinfectants and it is possible that they may survive even after disinfectant measures are taken [22].

In our research, Micrococcus was the fifth most common microorganism observed on nurses' cellphones (10%). This type of bacteria is observed everywhere such as in water, dust, and sand. It is the voluntary resident in natural skin flora and devices or equipment not properly cleaned and disinfected are where we can find it [23].

Non-hemolytic streptococcus and Enterococcus were observed in 2 mobile phones (6.7% each) owned by nurses studied in our research.

Non-hemolytic streptococcus is a kind of the bacteria in natural flora of human skin and it is one of the most frequent bacteria in the upper respiratory tract and conjunctiva of human eye and rarely causes any diseases for humans [24].

The least frequent microorganism observed on these mobile phones was Klebsiella observed on only 1 mobile phone (3.3% of cases).

Klebsiella species, particularly K. pneumoniae, are important members of Enterobacteriaceae family. They are considered to be opportunistic pathogens associated with acquired hospital infections such as neonatal infections, septicemia, pneumonia, urinary tract, and wound infections [25].

The following pathogens were observed on the surface of the mobile phones of therapeutic staff (doctors, nurses, residents and interns) in the research conducted by Karabay et al [1]: E. coli (40%), Enterococci, E. faecalis (20%), Pseudomonas aeruginosa (20%), Pseudomonas fluorescens (10%) and Klebsiella pneumoniae (10 %).

The following bacteria were found on the mobile phone of medical nurses in the study conducted by Tagoe et al [13]: 23% Bacillus cereus, 19% P. mirabilis, 3% Salmonella, and 2% Shigella. The most common pathogen observed on the mobile phones of workers in health centers in the study of Sepehri et al [14] was S. epidermidis (23% of all mobile phones). In the study carried out by Sridhar et al [26], the following values were found for each contamination in mobile phones: 46% with Microccus, 8% with coagulase-negative Streptococcus, 5% with S. aureus, 1% with P. asturiensis, 2% with Acinetobacter baumannii, 1% with Citrobacter frondii, 3% with Klebsiella oxytoca, 2% with non-albicans candida, 1% with trichosporonosis, and 1% with Aspergillus niger.

Considering the questionnaires completed by participants, all the participants agreed with this view that mobile phones can act as transporters of microbes particularly hospital bacteria and that cleaning your mobile phone can help reduce spread of microbial agents. However, 16% of the participants never used to clean their phones even once a day. This is less than the rate reported reported in previous researches. In the research conducted by Ghardashi et al [27], 94% of therapeutic staff (doctors, medical students, nurses, paramedics) believed that mobile phones can act as transporters of pathogens but 44% of them never used to clean their phones. Although all nurses knew they had to wash their hands after routine activities in Morioka et al.'s research [28], 36% of them never washed their hands after using their mobile phones.

Keeping in mind the fact that as many as 16% of the nurses taking part in our research admitted they never cleaned their phones even once a day and since these nurses work in the ICU, their failure to observed with rules of hygiene may turn their phones into transporters of bacteria to the patients. As a result, it is recommended to use visual notes and educations (like brochures and posters) concerning cleaning their mobile phones and limiting their use in critical units and observing the rules of hygiene in hospital. This becomes even more important when we keep in mind that cleaning mobile phones results in significant reduction of contaminations.

CONFLICT OF INTEREST

The authors declare no competing interests in relation to the work.

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ARTICLE

SECURED OPTIMAL ROUTING BASED ON TRUST AND ENERGY MODEL IN WIRELESS SENSOR NETWORKS

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ABSTRACT

Objective: *In Wireless sensor networks, nodes have deployed to monitor and collect the physical or environmental condition and cooperatively pass the data to the main control node through the network. The data forwarded to the main control node should be efficient and trustable one.* ***Method:*** *In this method a Scalable Energy based Trust model for Security nodes and Data Encryption (SETS-DE) with the private key is proposed. The nodes have very limited capability so profound computations for security mechanisms are not suitable hence; the trust values of nodes are computed for security purpose by using its energy consumption value. The data collected from the sensor node is passed through the trusted nodes. Even though the trusted node might become malicious but the encrypted data cannot be hacked or modified by the corresponding node.* ***Improvement:*** *This proposed method improves the performance measures for packet delivery, throughput and efficiently reduces the energy consumption.*

KEY WORDS
Wireless sensor networks, Nodal energy, Trust based security, Single Message encryption,

INTRODUCTION

A Wireless Sensor Network (WSN) is a group of nodes structured into a cooperative network. Each node consists of processing capability, memory, a RF transceiver, a power source such as battery; solar cells etc., and accommodate various sensors and actuators. The nodes communicate wirelessly and often self-manage after been deployed in an ad hoc manner. Sensor nodes popularly used for monitoring several applications such as environment for battlefield surveillance, military, wild animals. These sensor nodes have severely restricted to resources such as energy, memory and computational power.

In a typical WSN application, the sensor nodes spread in a region from where they collect data to achieve certain goals. Data collection may be a continuous, periodic, or event-based process. The WSN must be very stable in some of its applications such as security monitoring and motion tracking. Systems of 1000s or even 10,000 nodes were anticipated to process an application. Security and privacy are critical services needed for these systems. Security is a broadly used term encircling the characteristics of authentication, integrity, privacy, non-repudiation, and anti-playback. When the dependency on the information provided by the networks has been increases, then the risk of secure transmission of information over the networks has also increased.

To protect WSNs against malicious and selfish behavior, various methods of secured routing protocols had developed which mainly rely on cryptographic basics and authentication mechanisms. Nodes in the network may be compromised due to lack of energy and performs malicious attacks such as packet droppings and packet modifications to disrupt the normal operations of sensor networks.

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RELATED WORK

Multi-hop relay had proposed to enhance the coverage area and to forward traffic effectively between the (Base Station) BS and the (Mobile Station) MS consists of several intermediate mobile nodes in between. The novel technical solutions and algorithms for multi-hop relay is analyzed, including the separation of control and data, effective signal-to-interference-plus-noise ratio (SINR)-based routing algorithms, and cooperative relay schemes. Several techniques were proposed but energy consumption is higher for processing the data during transmission. Dynamic Source routing protocol had proposed in multi-hop wireless ad hoc networks, which is composed of the two mechanisms such as Route Discovery and Route Maintenance. This two mechanisms work together to allow nodes to discover and maintain source routes to arbitrary destinations in the ad hoc network. Generally, routing mechanisms are selfish in nature, which leads inappropriate behavior in the network and leads to performance degradation in the entire network [1].

Optimal Forwarder based on Energy and Trust for Routing (OFETR) protocol had proposed to select and prioritize nodes forwarder list based on energy and trust value to improve the network lifetime. This protocol consists of Energy Watcher, Trust Manager and Optimal Forwarder to record the energy values, track the trust values and to address the problem of forward list [4]. Trust-based secure routing model had proposed in which micro Timed, Efficient, Streaming, Loss tolerant Authentication (micro TESLA) algorithm

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is used to ensure that the data should not be tampered by malicious nodes i.e. to authenticate the data packets between source and destination nodes [5].

A robust Trust-Aware Routing Framework for dynamic WSNs had proposed to provide protection against the identity deception through replaying routing information. TARF secures the multi-hop routing in WSNs against intruders misdirecting the multi-hop routing by evaluating the trustworthiness of neighboring nodes. It identifies such intruders by their low trustworthiness and routes data through paths circumventing those intruders to achieve satisfactory throughput [6].

A scalable cluster-based hierarchical trust management protocol for wireless sensor networks had implemented to effectively deal with selfish or malicious nodes. A trust management protocol is applied in which a SN may adjust its behavior dynamically according to its own operational state and environmental conditions. A SN is more likely to become selfish when it has low energy or it has many unselfish neighbor nodes around [7].

A highly scalable hierarchical trust management protocol for clustered WSN had proposed. Here each node subjectively evaluates other peers periodically. Peer to peer trust evaluations are reported from sensor nodes, a cluster head obtain trust report of all sensor nodes present in its cluster and this cluster head performs a statistical analysis to identify and exclude malicious node from the network. This trust-based IDS scheme considers the effect of both social trust and QoS trust on trustworthiness or maliciousness [8]. Scalable Trust Based Secure (STBS) [9-10] wireless sensor networks had proposed new components for trust management systems even there is a change in the network. When the new nodes deployed in the existing network, the trust relationship should be maintained between the newly deployed nodes and the existing nodes. However, maintaining scalable energy based trust relationship between the nodes in the network is difficult in this existing method.

Scalable energy based trust model for security nodes and data encryption

A novel and scalable energy based trust model for node security method with the encryption of data is proposed. Data Encryption Standard (DES) is applied to assure message passing security in this proposed method. Generally, nodes have limited capability and consume high energy for security purposes; hence instead of implementing heavy security mechanisms, a node based trust factor, which includes both energy consumption and selfishness factor, is designed. The nodes may break routes due to malicious action, malfunction, low hardware resources; and having low processing energy is all characterized as node behavior. The objective of this proposed model in WSN is to identify the trusted nodes and to pass the encrypted messages to the trusted nodes. By improving security and reducing energy consumption level improves the novelty of the proposed SETS-DE mechanism. Here, three-tier system such as Mobile Sink (MS), Access Point (AP) and Motes (M) are proposed in order to derive optimal routing, maximize the network lifetime and secure transmission of data.

Phase 1: Tier 1 to Tier 2

In this phase, RREQ is broadcasted from the source node present in the mobile sink to the intermediate node relies in AP. The threshold value ranges from 0.7 and 1.0 for AP and Motes. If the trustworthiness of the mobile node matches with the threshold value, then the AP transmits the request to the second phase.

Phase 2: Tier 2 to Tier 3

RREQ is passed from the intermediate node to the destination node present in the Mote. The mote has predefined threshold value. If the intermediate node's trust value matches with the predefined threshold value of the destination the RREP is sent via the same path.

Selfishness Factor

In this mobile sink phase, the source node sends the Route Request (RREQ) to the AP through the intermediate nodes. The trust model is proposed to calculate the trustworthiness of the each node present in the network and the trustworthiness factor for each node is evaluated by their residual energy. The node may change to malicious node due to lack of their residual energy. The malicious node in the network is identified by the selfishness factor. The selfishness factor can be derived by the ratio of RREQ to the number of Route Reply (RREP).

$$Selfishness\ Factor = {No\ of\ RREQ}/{No\ of\ RREP}$$

Energy calculation

It is necessary to calculate the energy level in each node in order to identify the average energy consumed by the nodes for the data transmission. This includes energy spent for sending, receiving and processing the data from mobile sink to destination via AP. The residual energy level in the node can be evaluated by using the below equation.

$$Energy\ consumption = Initial\ energy - Current\ energy$$

Nodal trust value

The trustworthiness of the nodes or nodal trust can be calculated by using two factors such as selfishness of the node and the available energy level of the node after processing the requests. It can effectively guide the data route in choosing nodes with high trust to avoid black holes.

$$Trust\ value = \Sigma_{i=0}^{n}(S_{reply_{(i)}} + Potential\ energy\ of\ the\ node_{(i)})$$

$$S_{reply} \succ Successful\ Reply$$

Algorithm for SETS-DE

Step 1: Broadcasts RREQ from SN to AP
Step 2: Identifying Trust value of each node
(a) Calculate Selfishness factor

(b) Calculate energy component

Step 3: Checks for the threshold value of AP
Step 4: If trust value matches with the threshold value, then the RREQ passes to the second phase.
Step 5: Again step 2 process continues
Step 6: If threshold value of intermediate nodes matches with the threshold value of Motes, then RREP is passed to the source.
Step 7: The trusted route had discovered, and data is sent via in this route from the source to the sink.
Step 8: The data is encrypted with private key, even the trusted nodes become malicious it cannot access the data.

Reliable data transmission

Once the reliable and trusted route is discovered, the data passed from the source node to destination node present between the tier 1 and tier 3. The data is encrypted with the symmetric key even the intermediate node become malicious, it cannot modify the information contained with it. To ensure the secured and reliable data transmission, the threshold values are fixed and verified for the intermediate nodes by the AP and the motes. The goal is to maximize the ratio of successful packets reaching the sink and to reduce the energy consumption. The data encryption Standard (DES) can be implemented by using the security key management technique.

SIMULATION RESULTS AND ANALYSIS

In order to analyze the performances of the proposed method SETS-DE, the packet delivery rate, packet loss rate, delay rate and throughput are compared through simulations with the existing method.

Packet delivery rate

The Packet delivery rate is the ratio of the total packets delivered by the sender node to the corresponding receiver node in the network. The equation for PDR is shown below, where n represent the number of nodes in the network.

$$PDR = \frac{\Sigma_0^n\ Pkts\ Received}{time} \quad (1)$$

Packet loss rate

Packet Loss Rate (PLR) is the ratio of the packets lost during packets transmission sent by the sender to their corresponding receivers. The fig 2 shows the packet loss rate for the proposed SETS_DE and the existing STBS. The packet lost rate is lower for the proposed SETS_DE mechanism. The equation for PLR is given below,

$$PLR = \frac{\sum_0^n PktsLost}{time} \quad (2)$$

Delay

Delay refers to the latency time between sent packets and the received packets. The delay is calculated by using the equation shown below,

$$Delay = \frac{\sum_0^n (PktRecvTime - PktSentTime)}{n} \quad (3)$$

Where 'n' represent the number of nodes.

The average delay is plotted and it is shown clearly that the delay value is low for the proposed model SETS-DE than the existing STBS method)

Throughput

Throughput is defined as the total number of successfully received packets. The average throughput is calculated by using the equation shown below.

$$Throughput = \frac{\sum_0^n Pkts\ Received\ (n) * Pkt\ Size}{1000} \quad (4)$$

The SETS-DE method has achieved greater average throughput when compared to the STBS mechanism. The security measures had improved the network performance greatly.

Residual energy

The amount of energy remaining in a node at the current instance of time is said to be as residual energy. A measure of the residual energy gives the rate at which energy is consumed by the network operations. Fig 5 shows the proposed scheme has higher residual energy compared to the existing method STBS

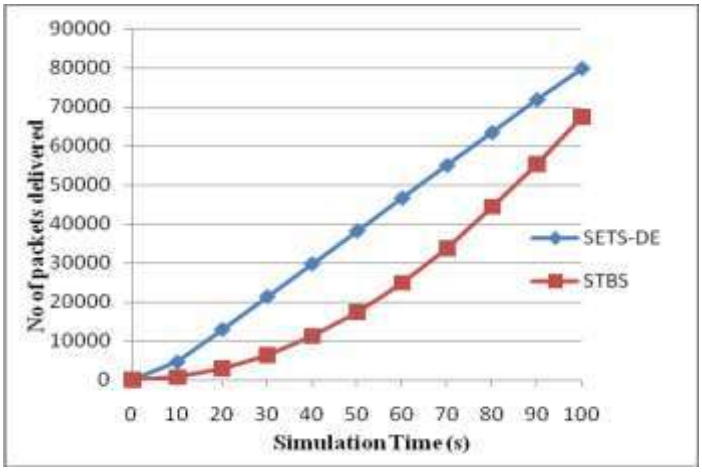

Fig: 1. Packet delivery rate.

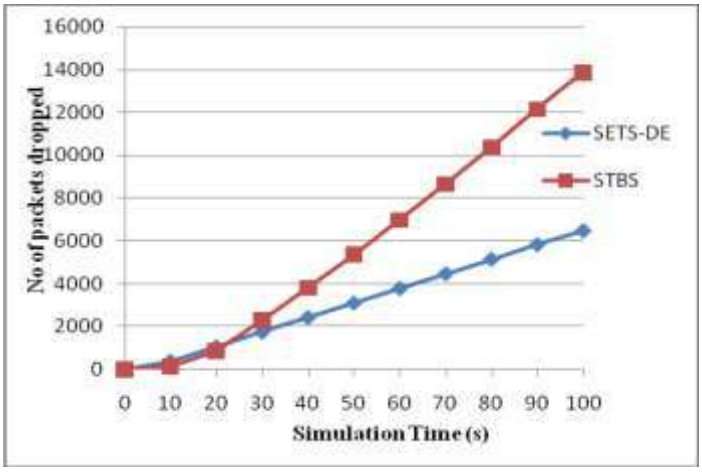

Fig. 2: Packet loss rate.

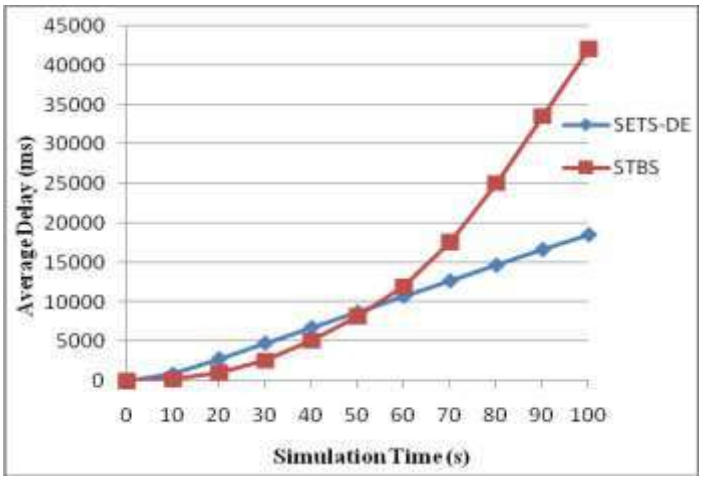

Fig. 3: Delay.

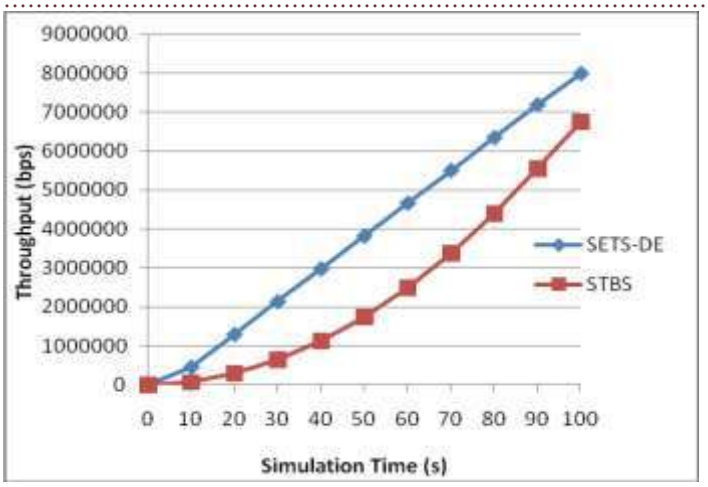

Fig. 4: Throughput.

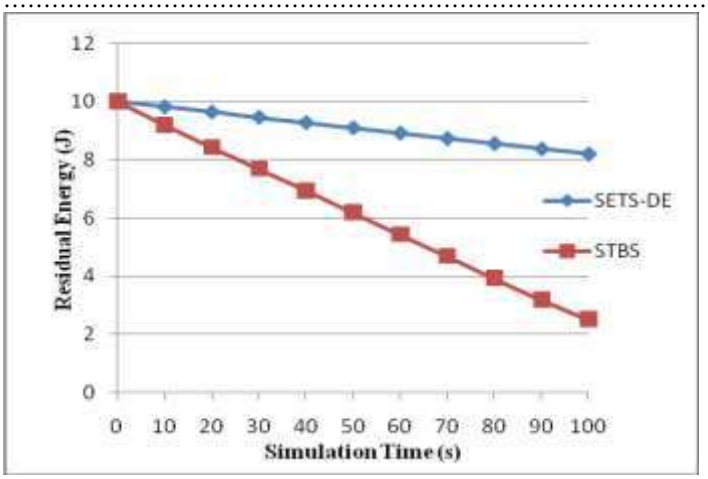

Fig. 5: Residual energy.

CONCLUSION

The Scalable Energy based Trust model for Security nodes, Data Encryption (SETS-DE) model is proposed for improving the scalability and reliability of wireless sensor networks in three tier based system. This proposed algorithm gives an efficient output in terms of energy consumption and trust based security nodes. This proposed scheme can be applied in high security requirement environmental scenarios. Simulation analysis shows better performance for packet delivery, throughput and average delay for the

proposed scheme is comparatively low. This improves the security in significant to the energy consumption of nodes. In future, the overall end-to-end delay can be further reduced by using secured energy based algorithms.

CONFLICT OF INTEREST

There is no conflict of interest.

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FINANCIAL DISCLOSURE

None

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ARTICLE

A CLINICAL TRIAL TO COMPARE THE EFFICACY OF STANDARD PRODUCTS OF ENTERNAL NUTRITION WITH CONVENTIONAL NUTRIENT SOLUTION TO IMPROVE THE PHYSICAL HEALTH IN DIABETIC PATIENT WITH ISCHEMIC HEART DISEASE

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ABSTRACT

Background: *CABG, Diabetic hospitalized patients show an increased rate in metabolic and catabolic processes, hyperglycemia, negative nitrogen balance, weight loss, muscle atrophy and multiple organ failure including gastrointestinal and respiratory failure. These events may be due to hormonal changes and the secretion of acute phase of the reactants. Therefore, this study aims to assess the effect of conventional nutrition in hospital (kitchen made), versus enteral nutritional therapy on several serum parameters in post-surgery diabetic patients to determine the preferred method to control these parameters.* ***Methods:*** *This prospective, randomized study was performed in a 14 months period on 35 diabetic patients between 18-72–years-old. The patients were randomly allocated into two groups to receive both conventional nutrition (Control Group) and enteral nutrition (Intervention Group). They were followed up for five days during admission in the hospital and after operation. In this study we have monitored the para-clinical parameters, such as fasting blood sugar (FBS), white blood cells (WBC), cholesterol, triglyceride, total protein, albumin & pre-albumin, blood urea nitrogen (BUN) and creatinine in three times, during their hospitalization. Also we have controlled their weight and general situation in mentioned period. The data were analyzed with SPSS version 18.* ***Results:*** *In our study some clinical parameters like: the concentration of serum albumine and pre-albumine in enteral group were significantly higher than control group. Also some parameters like: transferrin and total leukocyte count (TLC) were significantly lower in enteral group. By measuring these parameters, the count index showed the malnutrition in patients. As we used this Index in our study, malnutrition in intervention group (enteral), was significantly lower than control group.* ***Conclusion:*** *Some surgical patients need nutrition support for either pre- and or post-operatively due to the severity of their existing malnutrition or the presence of post–operative complications and hence prolonged delay in recovery of normal food intake. These patients should receive support by the simplest possible method using oral supplements, enteral tube feeding alone or mixed as necessary. In conclusion, the enteral method can provide more calorie and protein to post-operative, diabetic patients during their residency in hospital.*

KEY WORDS
Enteral Nutrition, CABG,Serum parameters, Ischemic Heart Disease, CONUT Index (Controlling Nutritional status Index).

INTRODUCTION

Although the history of utilizing enteral feeding procedure for hospitalized patients goes back to the 70's, attentions have just been attracted to its concept and utilization again. Malnutrition is a common problem in about 40% of the patients and due to the absence of an accurate monitoring system and lack of an appropriate metabolic support methods particularly for patients in critical phase, these patients are usually exposed to nutrition dangers [1].

Providing a correct and appropriate nutrition and diet therapy services in hospitals is an important factor that enhances the recovery of the patients, make it shorter and even prevents the diseases. According to researches, if nutrition as one of the main elements for patients' health be ignored in the hospitals or if it doesn't play its significant role in therapeutic process, it will cause dissatisfaction among the patients and disrupt the process of treatment. For instance, un-informed selection of foods that increase the levels of blood cholesterol in cardio-vascular patients and decrease the calorie and protein in patients with burning or infection or increase blood sugar in diabetic patients, will increase the critical conditions of the patients and decrease the effectiveness of treatments [2].

In other words, these patients mostly die due to the problems of malnutrition and not the disease itself. Nutrition is has an important role to prevent these kind of problems.

When the patient is not able to swallow or when he has no appropriate level of consciousness (such as those in the ICU) or when he is not willing to eat food due to nausea or anorexia (patients with cancer or after a hard operation), nutrition interventions are mostly carried out through vessels or intestines [3].

One of the target groups of the hospitalized patients with severe malnutrition are diabetic heart ischemic patients that is due to intestinal atrophy caused by micro and macro-vascular complications, a rising flow of malnutrition procedure is observed.

During the time of staying in the hospital and after operation (CABG), these patients have problems such as anorexia, unable of swallowing, digestive system failure and incomplete absorption of food materials. As a result of body's metabolic response to stress, more nutrition materials will be needed for body [4].

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The best nutrition strategy in this situation with minimum complication which can provide the body of the patient with the most controlled nutrients is enteral formula nutrients. In this method, all the body required nutrients and water with a fixed and controlled nutritional value are sent to the digestive system by some tubes through mouth or nose. Despite the kitchen made feeding, this method helps us make sure that certain food stuffs with a certain level reach the patient's body. This is also a better method in terms of hygiene and health [5].

Those patients who are in the danger of insufficient feeding (malnutrition) are as follows: Oncological patients, ear, nose and throat patients, patients with chronic inflammatory bowel complications, neurological patients, those with AIDS, elderly patients with mental problems, those with chronic liver and kidney failures before and after operation. There are special formulations for each condition and situation [6].

There are different enteral formulas and plenty of products for diabetic patients. These formulations contain less carbohydrates and more fat in compared with standard formulations. Of course, the source of carbohydrate in these formulations is quite different. These sources are oligosaccharides fructose, corn starch and fiber [7].

Considering the introduction of complementary food products to medication baskets and supplemental materials and increasing popularity of them, we tried to measure and estimate the efficiency of such products.

The aim of the present study is to compare the metabolic effects of enteral products among post-surgery heart ischemic patients with a history of diabetes and the kitchen made foods. Particularly, the metabolic support methods common in therapeutic centers are never conducted on a standard basis. Thus, the necessity of conducting such a research was completely clear.

MATERIALS AND METHODS

This random clinical trial study focused on the present state of diabetic patients undergoing CABG operation. The study lasted 14 months from March 2009 to May 2010 and it was conducted in Shahid Rajaie Heart Treatment and Education Center of Tehran.

Having studied the patients in terms of anthropometric parameters and collecting the medical history and conditions of inclusion in research, the patients were randomly divided into two groups. The first group (control) was fed on kitchen made food, while the second group (intervention) was fed on enteral foods.

Patients' inclusion criteria

1) The patient should be older than 18 and be hospitalized in men's or women's operation unit.
2) The patient should not be able to eat normally and only enteral feeding method could be used for him/her.

Patient's exclusion criteria

1) If the patient regains the ability to eat food while being hospitalized in the unit or during any stage of research.
2) If the patient dies or is discharged before the 5th day of his hospitalization.
3) Having liver or kidney problems.

The metabolic needs of the patients in intervention group were calculated individually according to Harris-Benedict equation:

TEE (men)=66.67+ (13.75×W)+(5×H)-(6.76×A)×Activity Factor×Stress Factor
TEE (women)=655.10+ (9.56×W)+(1.85×H)-(4.78×A)×Activity Factor×Stress Factor

The following codes were defined for the patients: A for age in terms of years, W for weight in terms of kilograms, and H for height in terms of centimeter. The activity factor for all those patients hospitalized in the hospital was set to ½. Each milliliter of the enteral solution contains 1/0 Kcal energy and in each 100 milliliter of solution, 83 milliliter of it is made of water. Having determined the daily level of TEE for each patient, the amount of the solution required by that person in one day was calculated and the amount of water and other liquids in it were determined. If the daily water required by the patient was more than what was supplied by the solution, this need was answered by adding an extra amount of water to the solution.

A group underwent enteral feeding (in the form of continuous feeding). This feeding was prescribed and conducted since the very first day the patient had entered the unit after operation.

It should also be noted that this clinical trial study was approved in the ethics committee of hospital of Rajaie Cardiovascular Medical and Research Center and all patients have been signed the secret consent form.

The patients in the witness group underwent Gavage according to the principles of Bolus in accordance with the usual procedure of hospital (without determining the amount of calorie required). The patients were studied and investigated during the five days period of research and study before operation, while eginning the feeding procedure (the first day after operation), the third and fifth day after operation in terms of serum albumin, pre-albumin, transferrin, total protein, serum lipids and fasting blood sugar (FBS)-blood urea nitrogen (BUN) and creatinine and Maastricht index and CONUT (PI prognostic index).

Maastricht Index = 20.68-(0.24 ×Serum Albumin (g/L)-(19.21 ×Serum pre-albumin (g/L))-(1.86 ×TLC (10 6/L))

Considering albumin indexes, number of total lymphocytes and cholesterol, a score would be given to the patients in count index [Table 1].

The method of calculating malnutrition using COUNT index:

Table 1: Assessment of under-nutrition degree by CONUT

Under-nutrition degree				
Parameters	Normal	Light	Moderate	Severe
Serum albumin(g/dl)	3.5-4.5	3.0-3.49	2.5-2.9	<2.5
Score	0	2	4	6
Total Lymphocytes/ml	>1600	1200-1599	800-1199	<800
Score	0	1	2	3
Cholesterol(mg/dl)	>180	140-180	100-139	<100
Score	0	1	2	3
Screening total score	0-1	2-4	5-8	9-12

SPSS version 18 (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc.) were used to analyze the data.

Quantitative variables were described in terms of mean ± standard deviation, while qualitative variables were described in terms of their percentage. One sample Kolmogorov-Smirnov test was utilized were used to study the trend line of data with normal distribution, Information analysis was conducted using t-tests, chi square, and repeated measure ANOVA models.

RESULTS

The clinical and laboratory assessments were completed in 35 patients. Two patients from the intervention group could partially recover their eating capability. Two from the control group and one from the intervention group passed away. [Table 2] shows the demographic information of the patients [Table 2].

Table 2: The demographic information of the patients studied

	Intervention group N=15	Control group N=15	P-value
Age (years)	60.43 ± 9.788	62.13 ± 8.096	0.615
Gender (male and female)	Male Female	Male Female	
Ideal weight (kg)	62.95 ± 14.55	69.16 ± 14.45	0.061
Primary BMI (kg/cm^2)	20.65 ± 5.05	22.78 ± 2.64	0.077

The changes in the serum albumin concentration was not significant in any groups (P-value = 0.30). The paired comparison of means between groups showed no significant difference (P-value > 0.05) [Fig. 1].

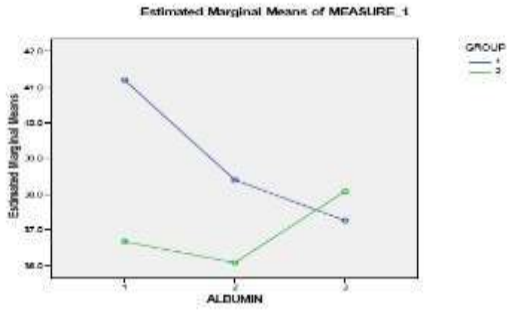

Fig. 1: Changes in the level of albumin in both groups over the course of time.

The general trend of pre-albumin changes during that period was significant among groups (P-value < 0.001). The comparison between the mean of this concentration in groups 1 and 2 demonstrated a significant difference with a P-value less than 0.001. Meanwhile, the mutual effect between groups and pre-albumin concentration was reported to be significant in various times (P-value < 0.001).

The trend of changing pre-albumin concentration from time 1 to 3 was not significant (P-value = 0.475), but the trend of change from time 1 to 2 and from 2 to 3 was significant (P-value < 0.001) [Fig. 2].

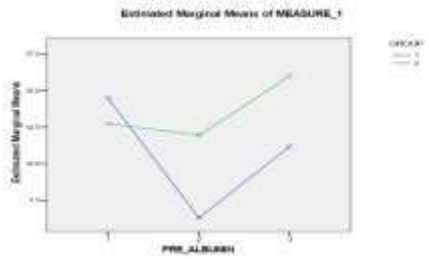

Fig. 2: Prealbumin changes in two groups over the course of time.

Total lymphocytes count was not significant while carrying out the research (P-value = 0.053). On the other hand, a comparison between the average total leukocyte count (TLC) of groups 1 and 2 showed no significant difference (P-value = 0.157).

The interactive influence of group and TLC was also reported to be significant (P-value = 0.02).

TLC changes over the courses of 1 to 2 and 2 to 3 were significant with P-values of 0.000 and 0.001 respectively. However, these changes were not significant in 2 to 3 period [Fig. 3].

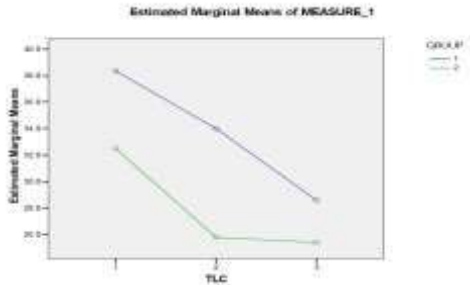

Fig. 3: TLC changes over the course of time.

Changes in transferrin concentration was generally significant without causing any distinction (P-value = 0.030). Comparison of its mean between groups 1 and 2 shows a significant difference (P-value = 0.05). Changes from period 1 to 2 and from 1 to 3 were also reported to be significant (P-value < 0.01). However, no significant change was observed from time 2 to 3. This means that transferrin in both groups was different [Fig. 4].

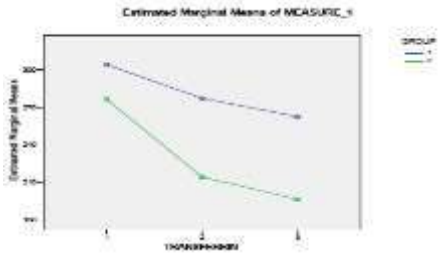

Fig. 4: Changes in transferrin concentration.

DISCUSSION

In the present study, the status of the patients receiving ready and sterilized solutions which contain a certain level of nutrition materials was studied in terms of pre-albumin (as one of the best parameters to determine the nutrition support adequacy), and deterioration of nutritional status (OUNT). Prediction of the state and reduction of the possibility of death indicated a significant improvement in compared with the patients who received hospital gavage. COUNT index seems to be an adequate tool to quickly diagnose malnutrition and constantly control the patient while he/she is hospitalized.

Due to economic and cultural causes and, above all, lack of awareness of the importance of nutritional state of patients, kitchen-made solutions under the title of hospital gavage are used for those patients who are in the recovery stage. These solution contain natural nutrition such as milk, egg, meat, juice and vegetables in puree form. Hospital staff think that these solutions are theoretically capable of fulfilling the nutritional requirements of patients. The studies conducted in this field do not approve this idea [8].

In a research conducted in Saudi Arabia (2004) by Mokhalalati et al, [9] 18 samples of the solutions prepared in three hospitals were studied and compared against samples of pre-prepared and commercial solutions in terms of nutritional content, pollution and microbes (including counting the aerobic micro-organisms developed in the plate and checking the growth of micro-organisms) and physical properties such as viscosity and osmolarity. There was a certain pollution in all samples of gavage (with differences between hospitals). These samples were observed less frequently in commercial samples. Viscosity of Kitchen-made (Gavage) samples was 200 times as much as what was observed in other samples and their osmolarity was reported to be twice more than other samples [9].

In the studies previously conducted to compare Enteral and Conventional methods, five studies reported changes in measurement of nutritional parameters. Three researches indicated an improvement in the health of patients (P=0.001 to P=0.05), while two studies did not report any change between the two groups. Another study had reported a significant reduction of death in enteral nutrition group (P = 0.02) [10-14].

This study showed a great frequency of malnutrition among post-surgery patients with a history of diabetes. It is recommended to form a team composed of doctor, hospital's pharmacist and a nutritionist in order to support the patients with appropriate nutritional support.

Thus, the present research aims to study the nutritional status of patients based on the above-mentioned criteria among two groups of people under standard enteral nutrition and compare it with those patients undergoing treatments with methods common in Iranian hospitals (using Kitchen made products).

CONCLUSION

Enteral nutrition can provide the patients having malnutrition with more protein and calorie compared to the usual nutrition and food of hospitals and improve the physical and health status of the patients. It will also result in a lower death rate and shorted period of hospitalization of patients. However, studies with a longer follow up period and more population are required in order to achieve more reliable results.

CONFLICT OF INTEREST
The authors declare no competing interests in relation to the work.

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FINANCIAL DISCLOSURE
There is no financial disclosure.

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ARTICLE

IN-VITRO ASSESSMENT OF ANTIFUNGAL EFFECT OF IBUPROFEN COMBINED WITH TERBINAFINE ON CANDIDA SPP

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ABSTRACT

Background: *One hundred and twenty-five throat swab samples were collected from the patient suffering from various disease conditions such as AIDS, cancer, diabetic and old age people. The healthy adult with no reported diseases were categories as control. Various species of Candida were identified using Gram staining, biochemical test and for the different species MIC was performed. The Candida species were also treated with ibuprofen as the cell wall integrity was affected because of it resulting in spheroplast. With the influence of the drug, minimum inhibitory concentration was estimated with Terbinafine that showed even in minor concentration of antifungal effect showed effective activity on the mortality of the Candida spp.* ***Methods:*** *The samples were screened for the presence of the Candida using plating. The organisms were confirmed using biochemical and Carbohydrate assimilation and fermentation test the organism were further tested with MIC with Terbinafine.* ***Results:*** *The Candida spp. cell were treated with the Terbinafine and effective MIC was shown, but when treated with ibuprofen the efficiency increased in the MIC results.* ***Conclusions:*** *When the Candida spp. cells were treated with Ibuprofen, the cell wall started to disintegrate that enabled the efficiency of the drug.*

KEY WORDS
Candida, Terbinafine, Ibuprofen, combined effect, spheroplast

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INTRODUCTION

Fungi had emerged as a cause of serious opportunistic infection among immuno-compromised and other critically ill patients, deep-seeded fungal infection were being recognized increasing frequency. *Candida* was recognized as one of the most frequent causes of opportunistic infections [1]. Ibuprofen was the first member of this class to be introduced in 1969 as a better tolerant alternative to aspirin [2,3,4]. They were analgesic, anti-steroidal, antipyretic and inflammatory efficacy is rated somewhat lower than high dose of aspirin which exhibit antimicrobial activity against *C.albicans* and non-albicans strains. Taking advantage of the drug's antifungal and inflammatory properties, the use of Ibuprofen along or in combination with Terbinafine [5] in the treatment of candidosis, particularly when applied topically,

In the present study attempt was carried out to isolate and identify the prevalence of *Candida* species among from different immune status people. Antifungal activity [6] was also studied by macro tube dilution method using Ibuprofen and Terbinafine.

MATERIALS AND METHODS

Selection of patients

Patients with AIDS [7], Cancer, diabetic, old age and adult with healthy medical record were acting as control group.

Sample collection

One hundred and twenty-five throat swab samples were collected with sterile wet cotton swabs (Hi-media Laboratories) that was moist by saline, the swabs were wiped over the thrust [8] under the supervision of medical practitioners with the written consent of the patients. The swabs were swabbed on the slant of SDA incorporated with Streptomycin. The samples were transported safely from the hospital/clinic to the laboratory where it was processed within 4 days.

Sample processing

SDA were prepared in Petri plates and the swabs were inoculated, the plates were incubated for 2 to 4 days at room temperature (28^{o}C).

Microscopic Observation
Gram staining

Kopeloff's & Beerman's modification of Gram staining was used to analyze morphological features of the *Candida* spp. cells.

Germ tube method

An isolated colony was touched and inoculated in human serum, which was incubated at 37^{o}C for 4 hrs. From that one loopful of inoculum was placed on the grease free slide and coverslip was placed over it and observed under 40 X magnification.

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Chlamydospore production

In Corn Meal Agar (CMA) plates, *Candida* spp. colony was inoculated into 3 parallel cuts made on agar. A cover slip was placed over it. Incubated for 18 to 48 hours. After incubation, the plates were examined through the coverslip under the microscope.

Carbohydrate fermentation test

An aqueous suspension of *Candida* spp. cells was prepared in saline, not to exceed the density of McFarland No.1 standard. 0.1 ml of this suspension was added to each of the fermentation broth tubes containing 1% peptone, 2 % sugar (Dextrose, Maltose, Lactose, and Sucrose) with bromo thymol blue indicator containing Durham's tube to detect gas production. The tubes were incubated for 10 – 14 days at 30^{o}C and observed for acid and gas production.

Carbohydrate assimilation test

Candida spp. suspension was prepared in saline equivalent to density of McFarland No.4 Standard. Using sterile swab the surface of medium was swabbed with *Candida* spp. suspension. Filter paper disc – prepared from Whatmann No.1 was impregnated with 20% solution of sugar (Dextrose, Maltose, Lactose, Xylose, Sucrose, Cellobiose) was placed at certain distance on the medium. Plates were incubated for 2 to 4 days. Growth around each sugar indicated assimilation

Antibiogram [Broth Macro Dilution Antifungal susceptibility testing of *Candida* spp. (CLSI, USA –M 27A)]

Macro broth dilution Antifungal test (CLSI – M27A) was intended for testing *Candida* spp. that causes invasive infection. Antifungal agents (Terbinafine) which was purchased from Sigma and stored as manufacturer's recommendation [9].

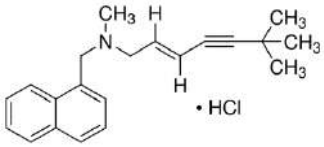

Fig.1: Molecular diagram of Terbinafine (trans-N-(6,6-Dimethyl-2-hepten-4-ylyl)-N-methyl-1-naphthylmethylamine hydrochloride).

The amount of powder or dilution need for the standard solution may be calculated by the following formula.

Volume (ml)=(Weight (mg) x Assay Potency (µg/µg))/(Concentration)

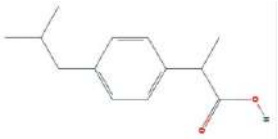

Fig. 2: Molecular diagram of Ibuprofen (2-(4-Isobutylphenyl)propanoic acid).

Ibuprofen was purchased from Cipla Pharmaceuticals Ltd. Mumbai. Ibuprofen (iso butry phyenl propionic acid) was diluted and the stock was prepared by ethanol. The diluent used was RPMI broth. Medium used was RPMI – 1640 (with glutamine, without bicarbonate and with pH indicator)

Inoculum preparation

Five colonies picked up from 72-hour culture, were suspended in 5 ml of sterile saline. The suspension was adjusted with McFarland No.0.5 used as stock. The MIC is the lowest concentration of an antifungal that substantially inhibit the growth of the organisms as detected visually [10].
Terbinafine - Sensitivity < 8 µg/ml; Intermediate 16 – 32 µg/ml; Resistance > 64 µg/ml

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Statistical analysis

The analysis was performed using SPSS version 17 software. P values < 0.05 were considered statistically significant [11].

RESULTS

The isolated organisms were categorized as [Fig. 3], that elucidate the distribution of different species of the *Candida*.
The identified organisms were used for performing MIC using Terbinafine, Ibuprofen and with combination.

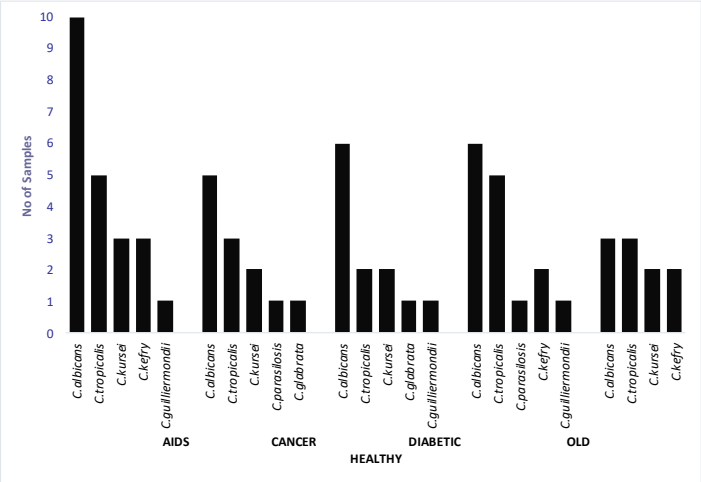

Fig. 3: Distribution of *Candida* spp. among different immune status patients.

ANTIFUNGAL SUSCEPTIABILTIY TEST

Table 1: MIC of terbinafine

Candida species	No. isolated	MIC of Terbinafine in µg/ml								
		128	64	32	16	8	4	2	1	0.5
C.albicans	30	4	5	7	5	4	2	2	1	-
C.tropicalis	19	-	2	2	6	8	-	1	-	-
C.kefyr	9	-	-	-	-	6	-	2	1	-
C.krusei	7	-	3	3	-	-	1	-	-	-
C.parapsilosis	2	-	-	2	-	-	-	-	-	-
C.guilliermondii	2	-	-	-	-	-	-	1	1	-
C.glabarata	2	-	2	-	-	-	-	-	-	-

The antifungal activity was performed on all the *Candida* species isolated from different groups of people showed the organisms were having effect on the Terbinafine at different concentration [Table 1].

Table 2: MIC of Ibuprofen

Candida species	No. isolated	MIC of Terbinafine in mg/ml								
		10	5	2.5	1.25	0.625	0.313	0.17	0.078	0.039
C.albicans	30	-	2	5	6	9	5	3	-	-
C.tropicalis	19	-	-	5	6	6	3	-	-	-
C.kefyr	9	-	1	2	2	3	1	-	-	-
C.krusei	7	-	1	2	2	2	-	-	-	-
C.parapsilosis	2	-	-	2	-	-	-	-	-	-
C.guilliermondii	2	-	-	2	-	-	-	-	-	-
C.glabarata	2	-	1	1	-	-	-	-	-	-

The effect of Ibuprofen showed that the organism became insubstantial cell wall that enhances the penetrability of the other antifungal drug leading to the destruction of the organism that was proved in the combination of the ibuprofen and terbinafine [Table 2].

Table 3: MIC of terbinafine combination of ibuprofen

Candida species	No. isolated	MIC of Terbinafine in µg/ml								
		64	32	16	8	4	2	1	0.5	0.25
C.albicans	30	4	2	4	5	7	4	4	-	-
C.tropicalis	19	3	2	4	2	2	2	2	2	-
C.kefyr	9	-	1	2	1	1	3	1	-	-
C.krusei	7	1	2	2	-	1	1	-	-	-
C.parapsilosis	2	-	1	1	-	-	1	-	-	-
C.guilliermondii	2	-	1	1	-	-	-	-	-	-
C.glabarata	2	2	-	-	-	-	-	-	-	-

Table 4: MIC of Ibuprofen combination of Terbinafine

Candida species	No. isolated	MIC of Terbinafine in mg/ml								
		5	2.5	1.25	0.625	0.313	0.15	0.078	0.03	0.01
C.albicans	30	-	-	4	11	9	5	1	-	-
C.tropicalis	19	-	-	2	8	3	4	2	-	-
C.kefyr	9	-	-	4	4	3	1	-	-	-
C.krusei	7	-	1	1	3	-	2	-	-	-
C.parapsilosis	2	-	-	-	2	-	-	-	-	-
C.guilliermondii	2	-	-	-	1	1	-	-	-	-
C.glabarata	2	-	-	-	1	1	-	-	-	-

Tugut et al., [12], Al-Athel et al., [13] and Alves Izabel Almeida et al.,[14] reported the effect of different drug that has an effect on *Candida* growth and enhance the effect of antifungal activity. Comparing the pervious result the significance of the combination of two different drugs had more influence on the control of *Candida*.

CONCLUSION

One hundred and twenty-five samples were collected from different categories of patients and healthy individuals to analysis the presence of *Candida* species. In AIDS patients, total number of positive samples was 88% in which *C. albicans* was about 45% followed by *C. tropicalis* – 23%. In Cancer patients, total number of positive samples was 48% in which *C. albicans* was about 41% followed by *C. tropicalis* – 25%. In Diabetic patients, total number of positive samples was 52% in which *C. albicans* was about 47% followed by *C. tropicalis* – 23%. In Old aged, total number of positive samples was 60% in which *C.albicans* was about 45% followed by *C. tropicalis* – 33%. In healthy persons, total positive sample was about 40%. Other strains isolated from the above categories were *C. krusei, C. kefyr, C. parapsilosis, C. guilliermondii* and *C. glabrata*. Minimum Inhibitor concentration (Macro dilution) done for Terbinafine, Ibuprofen alone and in combination with different strains of *Candida* reveal that they were highly susceptible when ibuprofen was diluted in the constant amount of Terbinafine when compared with that of Ibuprofen alone. From the above experiments, it proves that Ibuprofen does not inhibit the activity of Terbinafine, in turn induces the effect over *Candida* species.

CONFLICT OF INTEREST
Authors declare no conflict of interest

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None

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ARTICLE

AUTOMATED MOBILITY SUPPORT SYSTEM FOR BEDRIDDEN PEOPLE

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ABSTRACT

Now a days, in many home care centers where the nurses or care taker will supply the medicine and proper food to the patients time to time but usually the home care centers are not afforded by all the people. The proposed research is to provide better service for the patients, kids and the aged people. The support system is provided with DC geared motors which is controlled through android app or voice command. The support system is mobilized by the needy for supplying medicine, food and other supplies. This makes the aged and the bedridden patients partially independent. The system is designed with open source development board, Bluetooth module for communication between the system and user mobile and a suitable android app for controlling and monitoring the environmental parameters. The heart of the proposed research is controller and the smart Bluetooth which direct the geared DC motors to predefined path through the suitable motor driver. The components which are used in the design were simple and easily available which promotes easier construction and design. This design can also be used in hospitals that makes the people independent to get the needs of patient time to time.

KEY WORDS
Smart Trolley, Patients, Controller, Smart Bluetooth Kit, Atmospheric Condition

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INTRODUCTION

The main objective of the project is to serve bedridden people who are completely dependent on their care-taker. Now a days there are many home care centres where nurses or some care taker are sent to the needy by hiring them. Usually these home care centres are not afforded by all the people as it becomes a little costlier. This research provides an opportunity for the person who in need of medication, food and other supplies time to time on the daily basis making them partially independent by reducing the work load of the care taker. As it comes to a daily basis system, the person knows well about the time of the medication and other required supplies for them and accesses the device by using various option provided by automated mobility system. Sometimes it becomes difficult for the care takers who is one of the family member mostly to provide service in their work busy or they tend to forget to provide medicines, in such cases this automated mobility system helps the care taker to serve the needy.

The present hospital service system in India definitely needs an improvisation. The focus of hospital managements on to improve on all the aspects of the patients care and satisfaction [1]. A food/medicine delivery system must be hygienic and quality in hospitals which has definite beneficial effects on the recovery of patients and their quality of life [2]. Nutritional and Aesthetic quality is preserved throughout the service time by using a food trolley [3]. The trolley method of food distribution enables all foods to have a more acceptable texture and temperature than the plate system of delivery in hospitals. Patient's acceptance of served food is more towards the food served using food trolleys than the other [4]. However, with the trolley system patient satisfaction was improved, where 94% of patients were satisfied compared to 77% with the plate system. This indicates that nutritionally, the method of meal and medicine delivery is immaterial but patients do prefer choice at the point of consumption [5].

This automated mobility system is very easy to access and it is provided with an open source application where one can easily make use of the device. The automated mobility system consists of a trolley which is the main equipment used for serving the bedridden people or the needy. It can also be used to serve old people having difficulties. The device is operated through an app which is connected to the equipment through Bluetooth. The trolley is sent from one place to another which is a predefined path. On reaching the destination alerts the care taker for the supply. There is enough time provided at the destination to place the supplements on the trolley and the trolley comes back the original place that is to the patient or to the needy. The time taken to travel and the halt time are predefined. There can be as many different paths to travel say room-1, room-2 and so on. The trolley is also provided with shelf where the frequent requirements are also kept. Being easy to operate by all age people with various option provided it is adapted easily and bought into use. The whole equipment is a single trolley device and an app in your phone or tablet.

Objective

The proposed project is designed to provide better service for the patients, kids and aged people. It consists of a trolley provided with DC geared motors which is controlled through Android App or Voice Command. The trolley is sent and received where it is utilized by providing the needy by medicine, food and other supplies. This makes the aged one or the needy partially independent, still there must be a person to place the supplies on the trolley.

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SYSTEM ANALYSIS

Existing system

In present situation, the nurses from the care centre provide medicines and food for the aged or bedridden people. It is not sure that the medicines are going to them on time [6]. If in some emergency cases, the nurses will forgot to give the medicines. In some cases like if the bedridden people needs some water or something else immediately they cannot call the nurses at that instance. Some people doesn't prefer these care centre due to insecurity. The conventional trolley [7] which is used for supplying medicines or food in hospitals and care centres are shown in figure 1.

Fig. 1: Traditional Mobility System.

Problem statement

The objective of this project is to help the aged and disabled to carry out their chores. This uplifts their courage to work on their own; while reducing the workload of the caretaker simultaneously. In a manner, it turns out to be more efficient for the people under life term medication, as it can deliver their medicines on time and at regular intervals. We provide the model to serve them better and providing 24x7 monitoring in special wards by also supporting the caretaker with the needs to help the needy [9].

Proposed system

Block diagram

The block diagram is shown figure 2 which gives the detailed explanation about the mobility system. The central processing unit is arduino uno development board which processes and controls the system very effectively and accurately. The distance sensor is used as obstacle detector which alerts the person while the system travels through the predefined path. The bluetooth is connected to the development for the effective communication between the board and the user mobile. The optional feature also included in the system that user can operate the device without using smart phone through voice command. For recognizing voice command, voice recorder and voice recognizer is also attached with the controller. The motors cannot be driven directly by the controller since the controller will deliver the low level digital signals. So that the system is provided with the suitable motor driver depends on the rating of the DC motor. The integrated sensor unit called WICED sensor is connected with the processing unit for condition monitoring [8] of the patient room remotely.

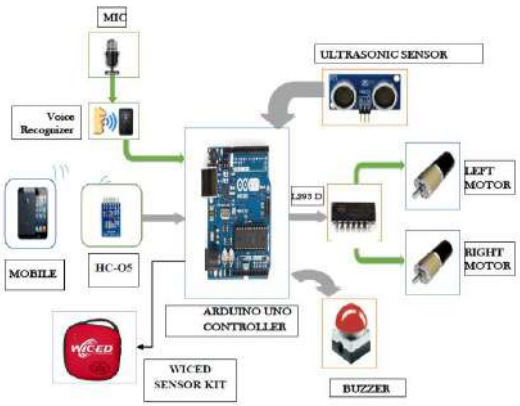

Fig. 2: Block Diagram of Proposed System.

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SYSTEM IMPLEMENTATION

Hardware

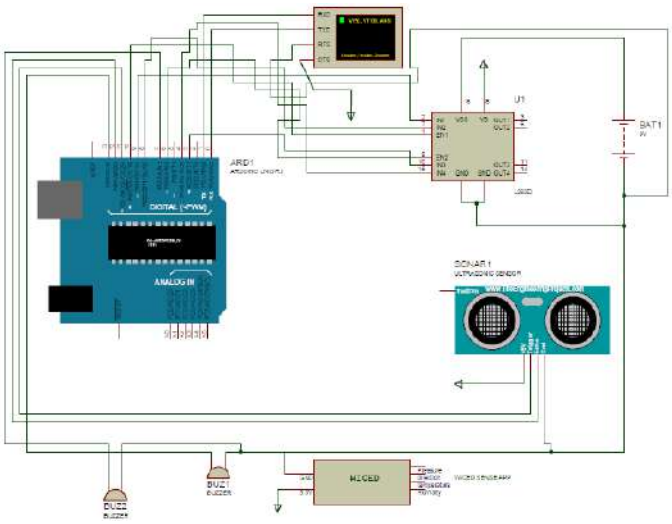

Fig. 3: Schematic and Wiring Diagram of the Proposed System.

The schematic and wiring diagram is shown in figure 3. Arduino Uno development board is selected as controller because of open source platform and for easy programming. The power switch on the trolley is pressed once, the device is ready to pair with smart phone or a tablet through bluetooth. The WICED sensor will be activated and start to monitor the environmental condition and the data's are transferred wirelessly.

The device is controlled through android app which is installed in user mobile phone or tablet and condition monitoring is done in nursing station. The device also controlled with the voice recognizer. The voice recorder will record and store the voice of the patient and recognizer will sends the analog signal to the controller according to the voice command. Once the Arduino receives the command through the serial port, it start to processes and the respective digital signals is sent to L239D and the DC motors are driven accordingly. L298D motor driver has the ability of controlling the motor in both forward motoring and reverse motoring.

In addition to that a couple of buzzers are connected to the digital pins of the controller for alerting the person to keep the needs on the trolley and alerting if any obstacles in the travelling path of the trolley. To provide an additional information like pressure, temperature, humidity of the patient room, WICED smart sensor is connected which will process the parameters and sends the data wirelessly to the nursing station.

The travelling path of the trolley is fixed according to the distance of the patient's room. For instance, the patient or the person in need of supplies as pressed up arrow in the app, the corresponding serial data is received by the module HC-05 and transmits the same command to the arduino indicating that the trolley should be sent to the room 1.The Arduino processes the command for L298D to drive the motor. Now the time taken for the motors to drive 10 seconds in forward path and 2 seconds to turn left or right and again travels say 5 seconds to the destination. Once the destination is reached, the buzzer alerts the person or nurse to provide the necessary. In case of any obstacles in the travelling path the buzzer alerts with the help of the ultrasonic sensor connected to the controller. The range of the detection of the obstacles can be programmed in the arduino platform. The time for the stay of trolley in the destination is also pre-programed and returns to the person who is the bedridden person or the person who operates.

Software

Arduino open source platform

The Arduino Software (IDE) is open source platform [10] and it is easy to program and fetch it to the board. Arduino IDE runs on Windows, Mac OS X, and Linux. This software is written in Java language and based on processing and other open source software. The Arduino platform has become quite popular with people just starting out with electronics, and for good reason. Finally, Arduino provides a standard form factor that breaks out the functions of the micro-controller into a more accessible package.

The coding for the controlling and processing is fetched into the ATMEGA328P microcontroller with the help of breakout board called Arduino Uno. The controlling of motor and parameter monitoring statement is started in void loop() for infinite operation. The pin mode declaration and serial port communication is

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declared in void setup() for one time running on the controller. The variable declaration and pin mode configuration of the proposed research is shown in figure 4.

Fig. 4: Arduino Programming Window.

Motor Control Android application

In the proposed work, open source android application named as "ARDUINO BLUECONTROL" is shown in figure 5 is developed with the help of MIT app inventor. The app enables the smart phone to communicate with bluetooth module HC-05 and receives the command from the user. The various features are provided in the application for controlling the motor drive. The graphical user interface (GUI) is done with the arrow keys (like up, down, left, right) and buttons. The user can control the trolley with the help of integrated accelerometer in the mobile phone. For example, the right arrow key in GUI is used to give the command to the controller which enables the motor to drive to go patient room 1, upward arrow key is used for room 2 and etc.

Fig. 5: Android Blue Control App.

WICED sense application

WICED smart bluetooth sensor is connected with the controller to monitor the pressure, humidity and temperature. The parameters are monitored by WICED sense android app as shown in figure 6 which is preinstalled in smart phone. The WICED sense smart kit is embed with BCM20737S Bluetooth-SoC and five microelectronic sensors like gyroscope, accelerometer, e-compass, pressure, humidity and temperature. The bluetooth kit connects directly to the sensor with the controller. WICED sense application displays the real-time data from the sensors so that conditioning monitoring is done remotely in nurse station.

Fig. 6: WICED Sense App.

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EXPERIMENTAL RESULTS AND DISCUSSIONS

The entire setup as shown in figure 7 is made ready for the operation. The power button is switched ON and for testing purpose, three predefined paths are assumed. On interfacing the device with a smart phone using the bluetooth module HC-05, one can make use of the trolley or device. Three different cases/locations is shown in figure 8 are explained below.

CASE 1: Room 1

When the user instructs the trolley to travel to the room 1, the bluetooth module receives the command and is sends the serial data to the arduino for the further processing. Both the motors rotates in forward direction for 10 seconds and turns left by keeping a left motor off and right motor on for 2 seconds and further proceeds for 10 sec reaching the destination. The timing need to be adjusted according to the distance of the predefined path and also the speed of rotation of motor. It alerts the care taker by drawing the attention with sound produced by the buzzer. The buzzer sound is turned off after 5 sec and the trolley returned to the original position in the same travelled path.

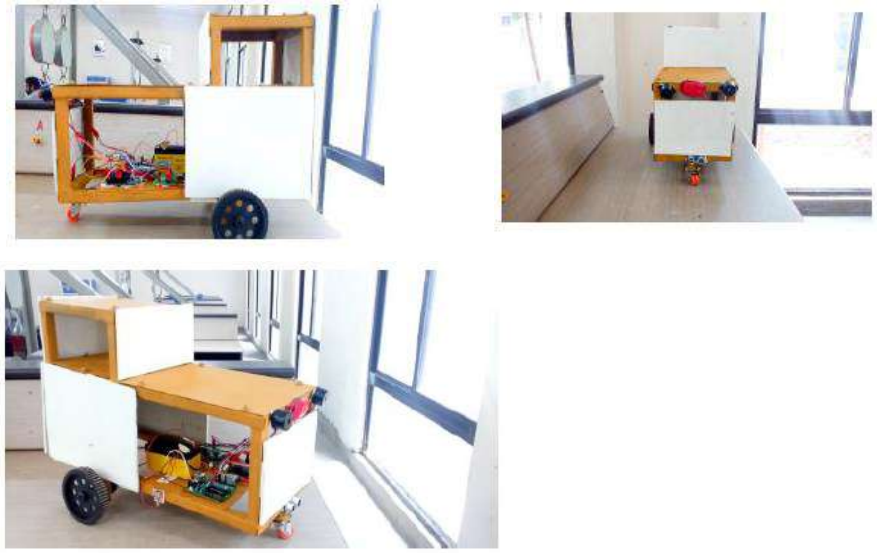

Fig. 7: Proposed Working Model.

CASE 2: Room 2

When the user instructs the trolley to travel to the room 2, the bluetooth module receives the command from the smart phone and sends the serial data to arduino for the further processing. Now the trolley is ready to go to room 2. Both the motors rotate say 15 sec in forward direction reaching the destination. It alerts the care taker by drawing the attention with sound produced by the buzzer. The buzzer sound is turned off after 5 sec and the trolley returned to the original position in the same travelled path.

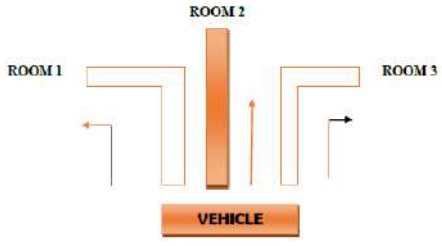

Fig. 8: Predefined Path.

CASE 3: Room 3

When the user instructs the trolley to travel to the room 3, the bluetooth module receives the command and send the serial data to arduino for the further processing. Now the trolley is ready to go to room 3. Both the motors rotate say 10 sec in forward direction and turns right by keeping right motor off and left motor on and again further proceed forward for 10 sec reaching the destination. It alerts the care taker by drawing the attention with beep produced by the buzzer. The buzzer sound is turned off after 5 sec and the trolley returned to the original position in the same travelled path.

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In all the cases, the WICED sensor will remains energized which will transfer the environmental parameters to the nurse station wirelessly. Since the trolley is intelligent, it will avoid and alerts when there is an obstacle in the predefined path. The effectiveness of the system is based on the quality of motor and type of the battery. The low cost battery like lead acid will drain at very fast rate and the performance of the system will be affected. Li-ion will be the best suitable for driving the trolley.

CONCLUSION

Using simple components available in the market, it is possible to invent new technologies. The developed product is to serving the need in both economic and efficient way for needy. It is similar to one serving the needy. Here developed a trolley travelling over all places of the centers/hospitals carrying supplies say food, medicines and other requirement from one place to another place. Keeping in mind to serve the needy in user friendly manner, a simple android application is used. This design can also be used in hospitals that makes the people independent to get the needs of patient time to time.

The trolley is used to travel in predefined paths which may require space moving in and around. The trolley mobilization is done on the basis of time which gives the less efficiency than the intelligent trolley. So, the proposed work may be extended by employing intelligence on the trolley in which the trolley is to be trained to mobilize the needs to the patient on time. The proposed model is designed for carrying the weight of 10 Kgs. The same concept may be extended to carry more weight by changing the rating of the motor and battery.

CONFLICT OF INTEREST
There is no conflict of interest.

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ARTICLE

GRAPH-BASED SENTENCE LEVEL SPELL CHECKING FRAMEWORK

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ABSTRACT

Spelling mistakes are very common on the web, especially when it comes to social media, it is much more common since (1) users tend to use an informal language that contains slang, and (2) the character limit defined by some social services such as Twitter. Traditional string similarity measurements (1) do not consider the context of the misspelled word while providing alternatives, and (2) do not provide a certain way to choose the right word when there are multiple alternatives that have the same similarity with the misspelled word. Therefore, we propose a novel sentence level spell checking framework that targets to find "the most frequently used similar alternative word". 146,808 sentences from different corpora are stored in a graph database. The similarity is calculated by using Levenshtein distance algorithm alongside the similarity between two given words. As the experimental results are presented in the discussion, the proposed framework is able to correct misspellings which cannot be corrected by traditional string similarity measurement based approaches. The accuracy of the proposed framework is calculated as 84%. Since the proposed framework uses a slang dictionary to determine misspelled words, it can be used to correct misspellings in the social media platforms.

KEY WORDS
Spell check; string similarity; edit distance; social media; Twitter

INTRODUCTION

Spelling mistakes are one of the key areas that many software systems have been working on in order to correct them which is critical especially for the systems that are built-in semantics. Natural language processing and sentiment analysis are two research areas that need a proper solution to correct spelling mistakes. A meaningful sentence may become meaningless when a letter of a word that specifies the sentiment is misspelled. According to the recent report by Global Lingo [1], 59 percent of 1,029 participants would not use a company which contains obvious grammatical or spelling mistakes on its website or marketing material. Another result of the report is that 74 percent of the same participants tends to check the quality of spelling while visiting a company's website. There is also economic side of this issue especially when it comes to e-commerce companies that drive their all business through their websites. Spelling mistakes in product catalogs may prevent users to reach their targets since they search products through the search engines or the companies' own websites. According to the research by an online entrepreneur [2], spelling mistakes cost millions in lost online sales. The official reports, documents have no toleration for spelling mistakes since a single letter typo may be crucial and irreversible. For all those reasons, we propose a novel sentence level spell check framework that uses context-aware analysis to correct misspelled words. The main contributions of this paper are listed as follows:

- A novel approach which is based on context-aware analysis is proposed to correct spelling mistakes in order to provide not just syntactically similar replacements but also semantically too. The findings are discussed in order to shed light on the difficulties of spell checking.
- The database the proposed framework is constructed on is specifically selected as a graph database which not just provides constructing better data structure but also improves the overall system performance and makes the knowledge base more scalable.
- The proposed framework can be used to correct misspellings in social media platforms since it uses (1) a slang dictionary to be aware of slang, and (2) it is trained with various datasets which contain formal and informal sentences.

This paper is structured as follows: Section 2 presents the related works. Section 3 describes the material and method. Section 4 presents the experimental results and discussion. Finally, Section 5 concludes the paper with future directions.

RELATED WORK

VGRAM [3, 4] is a technique to improve the performance of approximate string queries based on choosing variable-length grams, which can be used to identify similar strings based on their common grams. Authors improved the proposed technique by providing some filtering and merging algorithms in order to merge inverted lists of grams generated by strings.

Various filtering approaches are proposed such as using relational database management system [5] to use approximate string join capabilities. Cohen [6] proposes a framework to integrate heterogeneous databases based on textual similarity and proposed a logic called WHIRL that reasons explicitly about string similarity using TF-IDF (frequency-inverse document frequency) term weighting. Grossman et al. [7, 8] propose an approach to represent text documents and their associated term frequencies in relational tables. They may boolean and vector-space queries into standard Structured Query Language (SQL)

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queries. Chaudhuri et al. [9] propose a new primitive operator called SSJoin which can be used to implement similarity joins based on a variety of textual and non-textual similarity functions.

Golding et al. [10] propose WinSpell, a context-sensitive spelling correction algorithm based on combining variants of Winnow, and weighted-majority voting. Since the work is proposed before the rise of social media and microblogs, it cannot be used to correct misspellings in social networking sites and microblogs as is not aware of slang used in these platforms. Also, unlike our work, their work is not expected to perform well for various domains since the training data differs from one domain to other. Unlike that, our knowledge base is specifically designed to contain corpus from different domains in order to propose a general spelling checking method.

Carlson and Fette [11] propose an approach based on memory-based learning techniques and a very large database of token n-gram occurrences in web text as training data. They use GNU Aspell [12], an open source spell checking library, to generate candidates for spelling correction alongside their own method. We generate candidates by solely using our knowledge base through the proposed algorithm which is based on the frequency of co-occurrence in the knowledge base, and our own similarity measurement between the candidate and misspelled words as it is discussed in detail in Section 3. That lets us define our own method to retrieve candidates from our knowledge base instead of a semi black box model which lets us extend our work in the future without any dependencies. The latest version of GNU Aspell, GNU Aspell 0.60.6.1, is released in July 2011 at the time of writing which is outdated especially when the new words that are arisen by the social media are considered. Our knowledge base can also be extended with data from different platforms when it is necessary.

Lapata and Keller [13] propose an approach based on the search engine Altavista (which is not available anymore, purchased by Yahoo! in 2003) to correct spelling mistakes through the retrieved search results. One advantage of this approach is that it removes the necessity to create a large knowledge base. However, Liu and Curran [14] report that this approach gives much lower accuracy than retrieving counts from a collection of web pages.

Unlike the related works, the proposed spell checking framework targets sentence level spell checking and correction which is based on a native graph data model and can also be used for the text in the social networking sites and microblogs since (1) It is trained with the corpora such as telephone dialogues, face-to-face speech to include the words specific to the informal language used in social media, and (2) unlike the related works, it considers slang such as "*ty*", "*lol*", "*cu*" as valid words which are commonly used in social media [15–17].

MATERIALS AND METHODS

Levenshtein distance

Levenshtein distance [18], also known as edit distance, is a metric to measure the similarity between two sequences by calculating how many atomic edits (i.e. insertions, deletions, or substitutions) are required to convert one string to another.

Sentence level spell check framework

The proposed sentence level spell check framework is a context-aware approach that corrects the misspelled word by considering the previous and following words. neo4j, a highly scalable open source native graph database, is used to create the required knowledge base for context analysis. Words of sentences are stored in a directed two-way graph database with using the `NEXT` and `BEFORE` relations. The `NEXT` relation is used to link the following word with the previous one, and the `BEFORE` relation is used to link the previous word with the following one. An example of how sentences are stored in the graph database is presented in [Fig. 1].

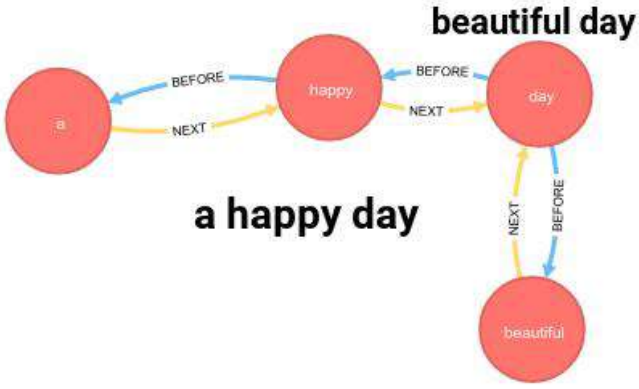

Fig. 1: An example of how sentences are stored in the graph database.

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46,808 sentences from Open American National Corpus (OANC) and 100,000 sentences from Leipzig Corpora [19] are imported into the graph database in order to create a general knowledge base that can be used with any domains. As a total, 142,685 words (nodes) and 4,053,733 relations are constructed to present these 146,808 sentences in the graph structure. The algorithm that is used to present sentences in the graph database is presented in [Fig. 2].

```
for each sentence in the corpora
   parse the sentence into the array of words
   find the previous (wp) and the following word (wn) to wi
   for each word (wi) in the array
      if wi already exists as a node in the graph
         create the relations between wp, wi, and wn
      else
         create the node to represent wi
         create the relations between wp, wi, and wn
      end if
   end for each
end for each
```

Fig. 2: The algorithm that is used to present sentences in graph database.

Spell checking and correcting

The proposed spell checking framework checks each word sentences in order to determine whether it is meaningful or not. This lookup is done by using the WordNet dictionary [20, 21], a lexical database for the English language that contains lexical categories such as nouns, verbs, adjectives, and adverbs, and also a predefined list of slang provided by Wiktionary, a project by the developers of Wikipedia. The latest version of WordNet, WordNet 3.0, defines 147,278 resources. If the word is not found in the WordNet database and the list of slang, it is supposed as a misspelled word and sentence level spell correcting process starts. The misspelled word is found in the graph database and its previous and following words are retrieved (if they exist). The graph database, neo4j, is queried by using the Cypher Query Language, an SQL-like declarative query language, which lets using two-way directed relations instead of writing traverses in the code [22]. Thanks to this ability, the following and previous words can be easily queried by just changing the direction of the relation. The similarity between each alternative and the misspelled word is calculated based on (1) the frequency of the usage of each alternative based on the previous and following words to the misspelled word, (2) string similarity measurement between each alternative and the misspelled word based on Levenshtein distance, and (3) number of common sequential letters between each alternate and the misspelled word. [Fig. 4] presents the method implemented using Java programming language in order to calculate common sequential letter count between two given strings.

```
private static Integer calculateCommonChars(String s1, String s2) {
    Integer commonLetters = 0;

    String bigWord = null, smallWord = null;

    if(s1.length() >= s2.length()) {
        bigWord = s1; smallWord = s2;
    } else {
        bigWord = s2; smallWord = s1;
    }

    for(int i = 0; i < smallWord.length(); i++) {
        int seqLength = smallWord.length() - i;
        for(int j = seqLength; j > 0; j--) {
            String tmpWord = smallWord.substring(i, i + j);
            if(bigWord.contains(tmpWord) && tmpWord.length() > commonLetters) {
                commonLetters = tmpWord.length();
            }
        }
    }

    return commonLetters;
}
```

Fig. 3: The method implemented using Java programming language in order to calculate common sequential letter count between two given strings.

Let s to be the calculated similarity between w_i and w_a, w_i defines the misspelled word, wa defines each alternative word which is looked up in the knowledge base (the graph database) through the co-occurrence with the previous and following words to w_i. lev(w_i, w_a) defines the Levenshtein distance between w_i

and w_a. com(w_i, w_a) defines the number of common letters between w_i and w_a. The formula to calculate the similarity between the misspelled word and each alternative is presented in [Fig. 4]. As it is seen in the formula, the similarity (s) is directly proportionate to the frequency of co-occurrence (freq), and the number of common sequential letters(com) but it is inversely proportional to the Levenshtein distance.

$$s(w_i, w_a) = \left(\frac{freq(w_i, w_a) \times com(w_i, w_a)^3}{lev(w_i, w_a)^3} \right)$$

Fig. 4: The formula to calculate the similarity between the misspelled word and each alternative.

RESULTS AND DISCUSSION

Finding the right word to replace the misspelled word cannot be found by using the methods based on solely string measurement without considering the context. [Table 1] presents some examples of misspelled words with the corrections based on the Levenshtein distance and the proposed method. As it is clearly seen in [Table 1], context-awareness is necessary to replace the misspelled word with the suitable word which is maybe not the most similar one in terms of string similarity. Also, when the string similarity based distances of the candidates are same, there is no certain way to select one of them as the replacement for the misspelled word while the proposed method does spelling correction even though string similarities of candidates are same thanks to the frequency of co-occurrence. The proposed method not just uses the string similarity measurement to correct the misspelled word but also reveals the contextual suitability of each alternative by considering its usage frequency with the previous and the following words to the misspelled word, the number of common letters between alternative and misspelled words, and the calculated Levenshtein distance between alternative and misspelled words.

Table 1: Some examples of misspelled words with the corrections based on the Levenshtein distance and the proposed method

Misspelling	Levenshtein Distance		The Proposed Method	
	Candidate	Levenshtein Distance	Candidate	Levenshtein Distance
Development faze	Faze	1	Phase	2
Crew custome	Custom	1	Costume	2
Radar sencor	Censor, sensor	1,1	Sensor	1
Wheter forecast	Whether	1	Weather	3
Academic celender	Calender	1	Calendar	2
Flaot warning	Float, flood	2,2	Flood	2
Psychiatric petienthe	Patience	2	Patient	3
Christmas presenthe	Present, presence	2,2	Present	2
First-quarter prophit	Prophet	1	Profit	2
Quate village	Quite	1	Quiet	3

Since we could not find a publicly available dataset which fits to evaluate the proposed framework, the proposed framework is evaluated with a list which contains 188 commonly misspelled English words alongside the correct ones shared by Wikipedia based on the three different lists [23–25]. Sample sentences that contain these misspelled words are found from a various of online resources such as microblogs, and social networking sites since they commonly contain spelling mistakes [15, 26]. The proposed framework is evaluated through these sample sentences and the accuracy of it is calculated as 84%. The knowledge base does not contain 14 words such as "*hors d'oeuvres*", "*memento*" of these 188 words. When these words are ignored, the accuracy of the proposed framework increases to 90.8%. Since the proposed framework uses context analysis during spell correction, it is evident that the accuracy of the proposed framework depends on the diversity of its knowledge base. This knowledge base can be extended in order to include more words by importing corpora that contain grammatically and semantically right sentences while keeping homogeneity of the data. When we analyze the false corrections, the following reasons are recognized: (1) Some words are not found in the knowledge base, and (2) some words are less similar but a lot more frequently used within the context of the misspelled word than the right replacement.

The data structure of the knowledge base is as critical as the diversity in order to query the data in the right way to the proposed algorithm. Graph databases are the perfect solution to store the data which contains bi-directional relations between entries as it happens for natural language sentences. Using a graph database not just provides constructing better data structure but also improves the overall system performance as Vicknair et al. report that neo4j performs significantly better than MySQL, a relational database management system, for full-text character searches [27].

CONCLUSION

Correcting misspelled words to make them meaningful is critical for the systems based on semantics. Since the traditional string similarity measurements do not consider the context of the misspelled word,

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they do not look for a suitable word in terms of contextual accordance. Therefore, we propose a novel approach to correct misspelled words by not just considering string similarity between words but also contextual similarity is also considered. Both previous and following words to the misspelled word are analyzed in order to find the most frequently used similar word to replace the misspelled word with the correct candidate. Thanks to this context-awareness, the proposed framework is able to correct misspellings that cannot be corrected by traditional string measurement based spell correction approaches as the test results presented in the discussion. According to the experimental result, the accuracy of the proposed framework is calculated as 84% which is promising and encourages us for future improvements. The knowledge base is stored in a native graph database in order to provide more flexibility and better performance while querying the context of the misspelled word. Also, using the direction property of the relations between nodes (words), it is possible to query the data in both ways without writing traverses in the code. Since the knowledge base contains corpora from face-to-face speech and telephone dialogues which are more informal compared to books, reviews, the proposed framework is aware of slang and optimized to check the spelling on the social media platforms.

The proposed framework is specifically designed to not have any external dependencies in order to be open for further improvements. As a future improvement, authors would like to use sentiment analyzing methods while finding the suitable alternative word to replace the misspelled one by detecting the overall sentiment of the sentence. Also, the knowledge base can be extended by importing corpora that contain grammatically and semantically right sentences which are common in social media. Finally, we would like to evaluate the proposed work with a bigger dataset.

CONFLICT OF INTEREST

Authors confirm there is no conflict of interest.

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ARTICLE

ESTIMATION OF PARKINSON'S DISEASE RISK BY STATISTICAL MODEL

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ABSTRACT

Background: *The constant progress and complexity of clinical and non- clinical treatment of Parkinson's disease (PD) become very tough to diagnose the disease. This may lead to delayed diagnosis, misdiagnosis and excessive medical cost. Rapid advances in diagnostic techniques have offered an effective way for tracking the different stages of the disease. This paper focuses the early PD diagnosis and its progression is estimated by Gama Amino Butyric Acid (GABA) concentration level with the help of Striatal Binding Ratio (SBR) values. SBR values of Caudate and Putamen (left & right) are calculated from Single Photon Emission Computed Tomography (SPECT) images as treated as input variables and the response variable is GABA concentration level. The mathematical model for GABA concentration level is developed by using the input variables like SBR values of Caudate and Putamen (left & right). The performance of the model is analyzed using ANOVA (Analysis of variance), normal probability curve and residual plot. The coefficient of determination (R^2) gives 99.3% of fitness rate with the regression line. The progression rate of PD is measured for three consecutive years and it is compared with the threshold value of GABA to find the severity of the Parkinson's disease.*

KEY WORDS
Parkinson's disease, SBR, level of GABA concentration, Mathematical model, progression rate

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INTRODUCTION

Parkinson's disease is a progressive movement disorder which constantly affects the mid brain neurons of human called substantia nigra. It is clinically defined by the major symptoms of resting tremor, rigidity, postural instability, bradykinesia, cognitive and psychiatric disturbances.The diagnosis of PD is easy when symptoms are full blown. But an accurate diagnosis is quite tough when the disorder is mild, which demands the formulation of an early detection technique for PD [1-3].The inhibitory neurotransmitter dopamine regulates and controls movements, motivation and cognition. Degeneration of these dopamergic nerve cells along the nigrostraital pathway affects the gait system of human, which in turn leads to Parkinson's disease [4].

SPECT images take the crucial role to discriminate PD patients from the healthy group by calculating dopamine deficit in Caudate and Putamen of the midbrain, even in the premature stage of PD. Thus, calculating dopamine deficiency (ie.SBR) in Caudate and Putamen of the human brain from the SPECT image is a valuable diagnostic tool for discriminating Parkinson's disease from the healthy control [5, 6]. Still the cases have high SBR value misdiagnosed as PD(supposed to be low) and the cases have low SBR value misdiagnosed as healthy control (supposed to be high). Hence the misdiagnosed rate is significant [3].

Gamma-Amino Butyric Acid (GABA) is also a most essential inhibitory transmitter in the central nervous system (CNS) and spinal card. GABA mediates pre-synaptic inhibition of primary blood vessels in the motor neuron system. The disturbances of the GABA concentration level in CNS influence the motor system [7]. Several neurological disorders including Parkinson's disease, anxiety, depression, insomnia, and epilepsy are negatively related with the level of GABA concentration in the human brain [8]. Hence the neurotransmitters dopamine and GABA are found to be a novel diagnostic tool for detecting PD.

The model that the log of the odds states how the variables are related with prediction of the Parkinson's disease. Hence formulating the mathematical model is a new approach to diagnosis PD. In statistics regression analysis focuses on the relationship between a dependent variable and one or more independent variables. Primarily it supports to understand how the dependent variable changes when any one of the independent variable is varied while the remaining independent variables are held fixed. When the regression analysis has considerable overlap with the field of machine learning, it can predict the various disorders. It is also used to realize how the independent variables are related to the dependent variable, and to investigate the forms of these relationships [9].

The machine learning techniques such as Multivariate Logistic Regression (MLR), Artificial Neural Network (ANN), and Support Vector Machine (SVM) are effectively used to formulate a prediction model for diagnosing neural disorders. Machine learning techniques consent with individual level characterization rather than group level characterization. Hence high level of clinical translation is obtained. MLR aims at the determination of probability based on SBR values, which classify the subjects into different risk categories. SVM finds the hyper plane in order to classify the subjects and high accuracy was achieved [10-12].

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In the present study, the level of GABA concentration of Parkinson's disease is calculated using SBR values. The developed mathematical model of GABA is to predict the early diagnosis of PD and its progression rate by using regression analysis. The developed model has potential to assist the clinician in the diagnostic process.

COMPUTATIONAL METHODOLOGY

PPMI Database

All PD subjects taken from the international PPMI database are in three stagesof Hoehn and Yahr (HY). The corresponding SBR values are taken for the analysis [13]. The SBR values are calculated as follows:
Iterative reconstruction was performed on SPECT raw projection data using hybrid ordered subset expectation maximization (HOSEM) algorithm. Iterative reconstruction was done without any filtering to ensure consistency of the reconstructions. The HOSEM reconstructed files were processed for Attenuation correction, which was filtered and normalized to get the same anatomical alignment. Striatal uptake count densities of the region of interest (ROI) were extracted and used to calculate striatal binding ratios (SBRs) for each region of the four striatal regions.SBR is calculated by PPMI as follows and compared with Occipital cortex region below the Putamen as reference region [14].

SBR= (target region/reference region) – 1 (1)

Where,
Target region: left caudate, right caudate, left putamen, right putamen.
Reference region: occipital cortex.

Statistical significance of SBR

All statistical analysis was carried out using Minitab software with 5% significant level (95% of confidence level). Histogram plots were drawn for three consecutive years and it is presented in Fig.1. The plots illustrate the different stages of SBR values distribution for Caudate and putamen (both left and right) of PD Patients. It also shows the amount of overlap between the three consecutive years. The overlap is higher in Caudate (left and right) than Putamen. Higher the overlap, difficult to discriminate the progress rate of the disease [3]. Hence the classification tool plays a major role as they integrate all the characteristics of disease, train the model and categorize them accordingly.

The level of GABA concentration

The gradual changes of neurochemical lead to PD in the human body. The GABA and dopamine in Caudate and Putamen is interrelated to measure progression of PD. From the literature [15] it is found that the threshold level of GABA for PD is 0.265µmol/g. If the measured GABA lies below 0.265µmol/g the cases are affected by PD. Similarly it lies above 0.265µmol/g it is a healthy control. The Level of GABA concentration is measured using radio receptor array.

Mathematical model

The mathematical model for the level of GABA concentration is framed using regression analysis, for investigating the relationship between the variables called SBR and GABA. It demonstrates the relationship between GABA, Y (called as response or output or dependent variable) and four SBR values $X_1 \ldots\ldots X_p$ (called as predictor or input or independent or explanatory variables).

The linear regression equation for GABA is:

$$Y = a + bX \quad (2)$$

Where, Y= Level of GABA; X= SBR used to predict GABA; a = the intercept; b = the slope.

Here, regression is used to estimate the qualitative effects of the variables, namely Caudate (left, right) and Putamen (left, right) upon the variable GABA [16]. The standard error (SE) of regression indicates that the observations are closer to the fitted line, and the following equation calculates it.

$$\text{Standard error (SE) of regression} = \frac{\sqrt{\Sigma(yi - \hat{y}i)2}}{\Sigma(xi - x)2} \quad (3)$$

Where,

yi is the value of the GABA, ŷi is estimated value of GABA, xi is the observed value of the SBR, x is the mean of the SBR, and n is the number of observations.

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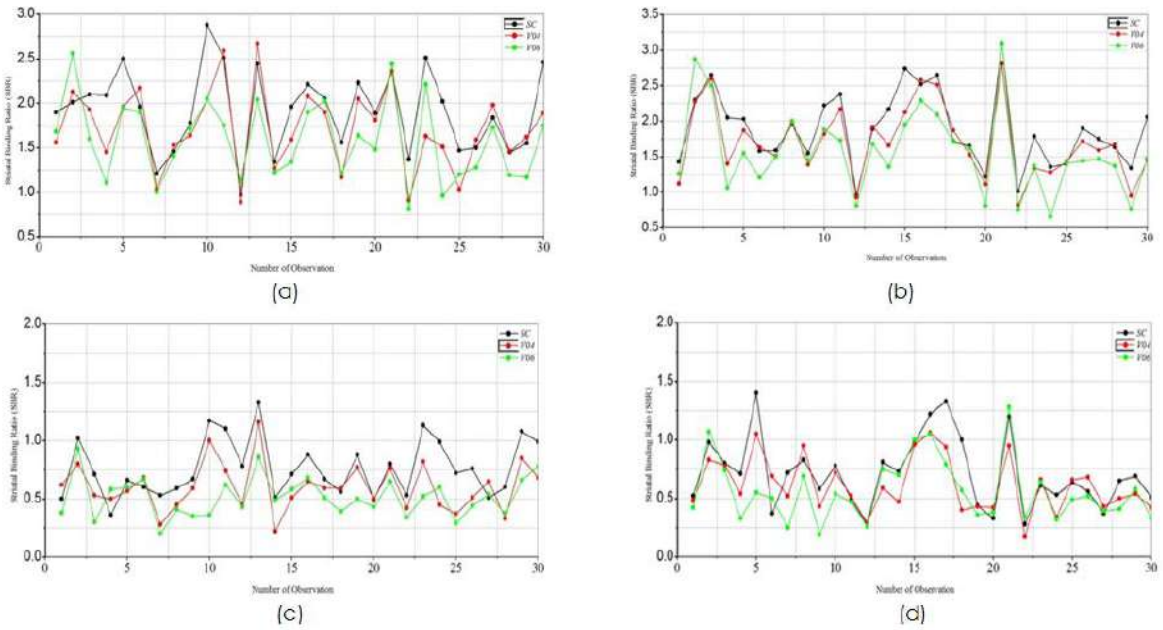

Fig. 1: Histogram plots of the striatal binding ratio (SBR) values for right caudate (a), left caudate (b), right putamen (c) and left putamen (d) for PD.

The p-value for each term tests the null hypothesis that the coefficient is equal to zero (no effect). A low p-value (< 0.05) indicates that the model is significant. And a high P-value (>0.05) indicates that the model is insignificant. The coefficient of determination (R-squared) is a statistical measure of how close the data are in the fitted regression line. R-squared is always between 0 and 100%. 0% indicates that the model has none of the GABA variables around its mean. 100% indicates that the model has all the GABA variables around its mean. In general, higher the R-squared, better the model that fits with the data.

RESULTS AND DISCUSSION

Formulation of the mathematical model for the level of GABA concentration

The coefficients of regression analysis of the level of GABA concentration for PD are shown in table 1 along with their P value of the parameters. It is observed that the P value of the level of the GABA concentration for Caudate (L) and Putamen (L) are most significant, whereas Caudate (R) and Putamen (R) are not so significant. It indicates the reliability of the model.

Table 1: Prediction time of parallel machines and prediction accuracy

Predictor	B	SE	T	P value
Constant	0.114468	0.005631	20.33	0.00
Caudate(R)	0.008960	0.004785	1.87	0.062
Caudate(L)	0.025654	0.004956	5.18	0.000
Putamen(R)	-0.005756	0.006367	-0.90	0.367
Putamen(L)	-0.028090	0.007518	-3.74	0.000

B is a regression coefficient for the predictors; SE is its standard error; T is test statistics; P value is the significance of the regression coefficient.

Where S is the estimated standard deviation about the regression line, R-squared is the coefficient of determination. Adjusted R-squared is an approximately unbiased estimate of the population R-squared.
The S value is the measurement of error.The model is better if it is smaller. The higher value of R-squared is better to determine the coefficients of a regression equation. The closeness of the adjusted R-squared with R-squared determines the fitness of the model [17]. In both cases, the adjusted R-squared value is closer to the R-squared value is shown in table 2.
The mathematical model given in equation 4 is framed from the coefficient (B) value of the regression table 1.

$$\text{GABA (PD)} = 0.114 + 0.00896 \times \text{Caudate(R)} + 0.0257 \times \text{Caudate (L)} - 0.00576 \times \text{Putamen (R)} - 0.0281 \times \text{Putamen (L)} \quad (4)$$

It is observed from the model that the GABA is positively related with SBR values of left and right caudate and negatively related with left and right putamen. Hence high value of putamen has less likely have PD.

Table 2: Summary of regression analysis

Responses	S value	R^2 (%)	Adjusted R^2 (%)
GABA for PD	0.0248413	99.3	98.7

S is the standard deviation; R^2 is the coefficient of determination; Adjusted R^2modified version of R^2

A high value of the determination coefficient (R2) confirms model adequacy, the goodness of fit and high significance of the model. This indicates that the regression models for the output can be used for determining and estimating GABA for PD.

Overall model evaluation

An analysis of variance (ANOVA) was performed for GABA to evaluate the model performance which is presented in table 3. The associated p-value for the model is lower than 0.05 (i.e. level of significance α=0.05, or 95% confidence), which indicates that the model can be considered statistically significant better than a null model.

Table 3 Analysis of Variance for PD

Source	DF	SS	MS	F	P value
Regression	4	0.059270	0.014818	24.01	0.000
Residual Error	355	0.219067	0.000617		
Total	359	0.278338			

DF is the degrees of freedom;SS is Sum of Squares; MS is Mean Squares;F calculated F value;P is a significance of regression coefficient

The normal probability plot for GABA is presented in Fig.2. It can be noticed that the residuals fall on a straight line, which means that the errors are normally distributed and the regression model is well fitted with the observed values. Fig. 3 shows the residual values with the fitted values for GABA. It indicates that the maximum variation of -0.075 to 0.050, which shows the high correlation that exists between fitted values and observed values.

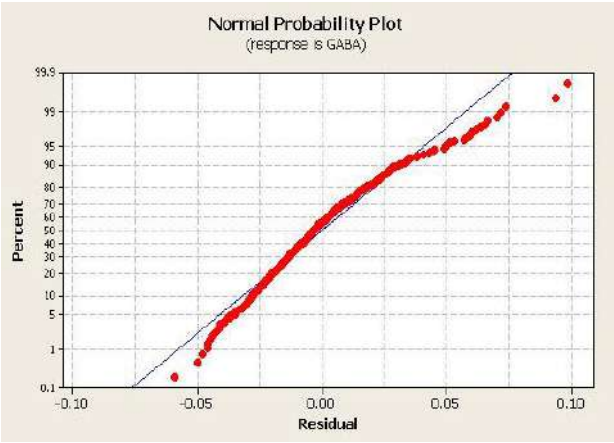

Fig. 2: Normal probability plot for GABA for PD

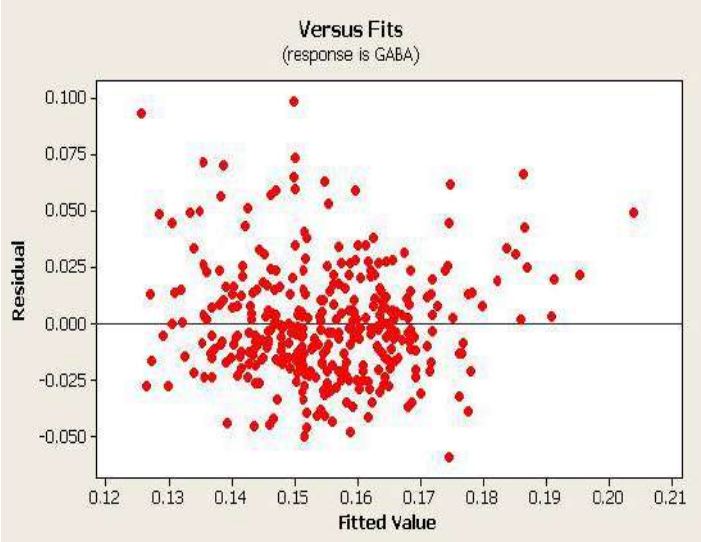

Fig. 3: Residual Vs fitted values for GABA for PD

Estimation of PD risk

The progression rates of PD for the three consecutive years are compared and its risk is shown in Fig.4. It shows less overlap between the GABA values, which has high discriminative power between them. The notched box plot shown in Fig.5 gives the outliers of the PD progression rate. Since all values lie between the ranges of the level of GABA concentration, it is evident that the high performance is observed from the developed model.

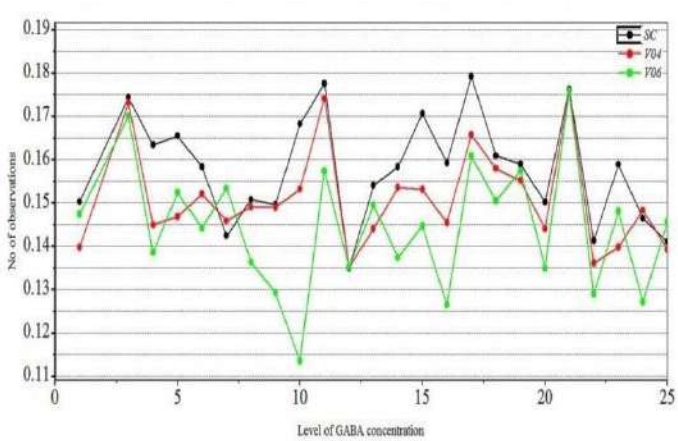

Fig. 4: Histogram plot for the level of GABA concentration

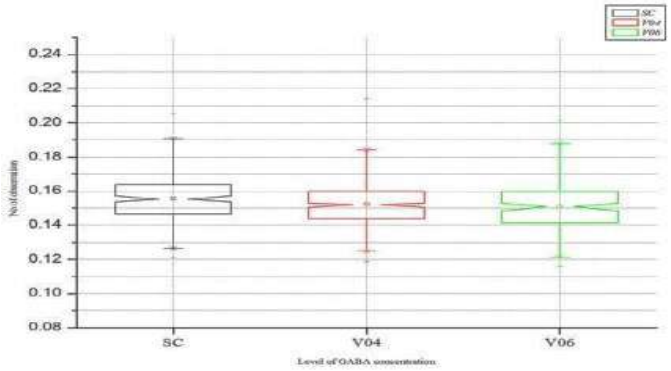

Fig. 5: Box plot for the level of GABA concentration

In each notched box plot, the central mark is the median (q2), the edges of the box are the 25th (q1) and 75th (q3) percentiles, the whiskers extend to the most extreme data points that are not considered outliers, and outliers are plotted individually. The extremes of the notches or the centers of the triangular markers correspond to q2 ± 1.57(q3 _ q1)/√n where n = 674 is the number of observations.

The SPECT images are again taken from the same patient for three consecutive years. The measured SBR values are applied to predict the early PD and its progress rate. The same procedure has been adopted for every three consecutive years to estimate the progression rate of PD. The Fig. 6 shows the progression rate of PD for three consecutive years. From the graph it is evident that the averaged GABA concentration level is increased for every year such as first year 0.1556, second year 0.15524 and the third year 0.1502.

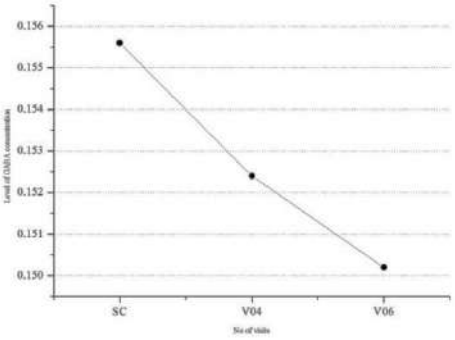

Fig. 6: Progression rate of PD

CONCLUSION

The diagnosis of early PD and its progression rate is estimated for three consecutive years. The predictive mathematical models for the level of GABA concentration of PD patients are developed by using Regression analysis. These models have the potential to discriminate PD from healthy control. The model performance was tested using ANOVA, normal probability curve and residual plot. The residual plots of GABA for PD are generated and it is observed that regression model is well fitted and highly correlated with the observed values. The progression rate is measured for three years from the model; hence, the severity of the disease is estimated. The inference is that the prediction models for estimating GABA concentration level is a novel method to aid the clinicians for diagnosing PD. It overcomes the misdiagnoses of PD with high rate of accuracy compared with the related work.

CONFLICT OF INTEREST

There is no conflict of interest.

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None

FINANCIAL DISCLOSURE
None

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