Global Advanced Research Journal of Medicine and Medical Sciences (ISSN: 2315-5159) Vol. 8(1) pp. 001-008, January, 2019
Available online http://garj.org/garjmms

Full Length Research Article

Study of the side effects of Docetaxel as chemotherapy medicine on changing the expression of genes of *Enterococcus faecalis* isolated from patients with breast cancer

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Accepted 15 January, 2019

The present study strived to ascertain the side effects of chemotherapy on the pathogenic potential of *Enterococcus faecalis* (a natural microflora bacteria) isolated from patients with breast cancer. Participants included 400 female sufferers from breast cancer before and after the period of chemotherapy and 400 healthy people living with patients.After RNA extracted from the stool of all the participants, cDNA was constructed. Nineteen virulent genes (*vanB*, *vanA*, *VanC-3*,*VanC-2*, *VanC-1*, *aac(6')-Ie-aph(2")-Ia*, *Tet(L)*, *Erm(B)*, *gelE*, *esp*, *gyrA*,*slyA*, *cylA*,*cylB*,*cylM*, *asa1*, *aggA*, *efaA* and *enlA*) of *E. faecalis* were assessed by Real-Time qPCR. The findings revealed a statistically significant correlation between the expression level of fourteen virulence genes(*vanA*(p = 0.033), *vanB*(p = 0.003), *VanC-3*(p = 0.003), *aac(6')-Ie-aph(2")-Ia*(p = 0.005), *Erm(B)* (p = 0.008), *gelE*(p = 0.002), *esp*(p = 0.0005), *gyrA*(p = 0.003), *slyA*(p = 0.001), *cylA*(p = 0.003), *cylB*(p = 0.0002), *asa1*(p = 0.003), *aggA*(p = 0.003), *efaA*(p = 0.003))in the group of the sufferers after chemotherapy and the other two groups (P<0.05).Additionally, the observation of patient group after chemotherapy showed an outstanding association between overexpression ofantibiotic resistance genes (*vanA, vanB, VanC-3, Erm(B), aac(6')-Ie-aph(2")-Ia*) and observation of the antibiotic resistance (vancomycin, erythromycin, gentamicin in respectively). Interestingly, while Docetaxel seems to be a suitable medicine to treat breast cancer, it may change the balance of mRNA expression of microflora. These could trigger infections during the cancer chemotherapy.

Keywords: Breast cancer, Docetaxel, antibiotic resistance, *Enterococcus faecalis*

INTRODUCTION

Docetaxel (Taxotere®) has been one of the most significant chemotherapeutic medicines used to treat cancer, was discovered in the 1980s (Kenmotsu and Tanigawara, 2015). A myriad of clinical studies showed that this drug was used for the treatment of various cancers. Docetaxel isolates from extracts of the European yew vegetation leave known as *Taxus baccata* (Pettersson et al., 2009; Ringel and Horwitz, 1991).In 1996, the US Food and Drug Administration (FDA) approved that the Taxotere® is suitable for using the topically advanced or metastatic breast cancer treatment after failure of the antecedent chemotherapy (Taguchi et al., 1994).

Breast cancer is the commonest cancers amongst females,and surgery combined with chemotherapy has been commonly utilized in breast cancer treatment (Li et al., 2014; Zhao and Rotenberg, 2014; Wang et al., 2015).The genesis or expansion of cancer is a multiple-step process triggered by the deactivation or activation of some of the cancer-associated genes through various pathways (Li et al., 2014; Zhao and Rotenberg, 2014; Wang et al., 2015). The surgical of breast cancer to remove the breast inevitably affects the quality of sufferers' life, due to chemotherapy is of critical significance in the treatment of early breast cancer. The various sensitivities of cancer sufferers critically limit the chemotherapy clinical result, due to infection mechanisms, antibiotic resistance, diverse pathogenic mechanisms, individual differences, and chemotherapy resistance (Wang et al., 2014; Jerjees et al., 2014; Gaule et al., 2014).

Although the chemotherapy may expand the patients' survival long, the betterment of patient quality of life is bound. Disturbance ofthe human microbial flora function is the most crucial side effects of cancer treatment method reported so far (Soha Sadeghi et al., 2018; Talebzade et al., 2018). One of the dysregulations may be linked to a reduction in the diversity of microbial rate and subsequent infection (Nicolatou-Galitis et al., 2006). Antibiotic resistance in the cancer sufferers with chemotherapy treatment is one of the most reported significant problems. *E. Coli* and *Enterococcus faecalis*are the most reported infections in these patients (Talebzade et al., 2018; Fijlstra et al., 2015; Seo and Lee, 2013; Liss et al., 2011; Hakim et al., 2018).

Enterococcus faecalis is a Gram-positive bacteria known as one of the most important Commensal microbiota of the human and other animal's intestinal Soha Sadeghi et al., 2018; Talebzade et al., 2018; Qin et al., 2010; Ocvirk et al., 2015; Tayebe et al., 2017). *Enterococcus faecalis* has the ability to become an opportunistic pathogen via acquiring several virulence genes such as the antibiotic resistance genes. Presence and changing of the virulence gene expression levels are significantly correlated with biofilm, infection, and antibiotic resistance in *Enterococcus faecalis* isolates. Therefore, it has been acknowledged as one of the most striking causes of nosocomial infections (Comerlato et al., 2013; Arias and Murray, 2012; Pinholt et al., 2014; Sievert et al., 2013; Semedo et al., 2003).

Some biological and environmental factors might trigger to alter the expression level of virulence genes of microbial flora (such as antibiotic resistance genes) (Lenz et al., 2010).

This research endeavoured to scrutinize the chemotherapy side effects on the microflora isolated from patients with breast cancer undergoing chemotherapy.

MATERIAL/ SUBJECTS AND METHODS

Subject selections and stool sampling

The Patient group includes 400 females with breast cancer, whichwere candidates for chemotherapy taking the docetaxel drug with a dose of 100 mg / m^2 every 3 weeks.The age range of 30 to 50 years, a healthy level of renal and hepatic functionality, and the hematologic status were the inclusion criteria.Thus, 400 healthy subjects which have been lived with sufferer at least for recent 12 months, participated. The purpose of this selection was that the kind of the microbial flora of the body is entirely associated with the lifestyle of the individuals. Likewise, age range and BMI in the normal group were matched with the patient group.The subjects with any infection or allergy have been excluded from the research. The demographic characteristics of the participants of the research are bestowed in Table 1.

The Research Ethics Board approved the protocol at Research Institute of Nikan Rooyesh Gene.The objective of the study was explained to all participants and wrote informed consent.

Gene expression study by quantitative Real-time PCR:

The viral RNA Mini Kit (catalogue number: 52906, QIAGEN®, USA) was used to extract Total RNA from faecal specimens of subjects. The quantity of extracted RNA was measured by Denovix Nanodrop device (Model Ds-11). According to Transcription of first strand cDNA synthesis kit (Revert Aid Premium First Strand cDNA Synthesis Kit #K1652, Thermo Scientific, Latvia), cDNA was synthesized. 16srRNA was picked as a housekeeping gene. "primer3" software was utilized to design Specific primers of the all studied genes. Real-Time PCR method was done by using Rotor-Gene 6000 (Corbett Research, Mortlake, NSW, Australia), and 2X RealQ PCR master mix with Green DNA I dye (Ampliqon, Denmark) according to manufacturer's protocol. In order to confirm *Enterococcus faecalis* species, the *E.faecalis* D-Alanine-D-Alanine Ligases (*ddlE.faecali*), which is a

Table 1. Demographic and clinical data for subjects participating in the study

Demographic and clinical data	Patient group with breast cancer	Healthy group
Participating	400 female	400 female
Age in year, mean (SD)	40±10	40±10
Marital status	Single :195	Single :180
Single / married / divorced/ widowed	Married: 102	Married: 92
	Divorced: 80	Divorced: 95
	Widowed: 23	Widowed: 33
Menopause at beginning of study (Yes/ No)	Yes: 38	Yes: 53
	No: 362	No: 348
Comorbidity (Yes/ No)	No: 400	No: 400
Breast cancer	One side:279	
One side/ two side	Two side:121	
Stage of cancer	Stage III	
Biopsy (Yes / No)	Yes: 223	
	No: 177	
Any surgery (yes / no)	Rhinoplasty surgery: 302	Rhinoplasty surgery: 242
	No: 98	No: 158
Radiotherapy (yes/ no)	No:400	No:400
Chemotherapy (yes/ no)	Yes:400	No:400
	docetaxel drug with the dose of 100 mg ⁄m2 every 3 weeks	
Hormonal therapy(yes/ no)	Yes: 101	Yes: 8
	No: 299	No: 392
infection	No: 170	No:400
	100 cases were resistant to vancomycin,	
	55 subjects were resistant to erythromycin, and 75 cases were resistant to gentamicin	

specific gene with the F:5-ATCAAGTACAGTTAGTCTTTATTAG-3.R:5-ACGATTCAAAGCTAACTGAATCAGT-3 sequence was used.

Statistic analysis

Descriptive datum has been shown as mean ± SD (limited area) and the statistical significance level has been set at $P < 0.05$. Altering gene expression among the surveyed groups have been examined by paired t-test and independent sample t-test. All assessments were done by SPSS version 22.

RESULTS

Table 1 shows Demographic, clinical and pathological data of patients.

Out of 1250 taken faecal specimens from participants, only 800 subjects were positive for the isolated bacterium belonged to the *Enterococcus faecalis*.

Gene expression results

Tables 2 and 3 present the descriptive statistics for the independent t-test and dependent t-test, respectively.

Table 2. *P-values* of *E. faecalis* microflora genes in patients before chemotherapy treatment vs. related normal subjects (p>0.05)

Gene	$2^{-\Delta CTCT}$	*P-values*
vanA	1.02	0.41
vanB	1.013	0.33
VanC-1	0.98	0.65
VanC-2	1.01	0.34
VanC-3	1.10	0.42
aac(6')-Ie-aph(2")-Ia	1.21	0.55
Tet(L)	1.04	0.087
Erm(B)	1.11	0.09
gelE	1.19	0.31
esp	1.15	0.092
gyrA	0.99	0.056
slyA	0.91	0.066
cylA	1.02	0.57
cylB	1.23	0.087
cylM	1.1	0.068
asa1	1.11	0.53
aggA	1.06	0.11
efaA	1.05	0.39
enlA	1.006	0.44

Table 3. *P-values* of *E. faecalis* microflora genes in after chemotherapy treatments vs. before chemotherapy treatments (*P-values*<0.05)

Gene	$2^{-\Delta CTCT}$	*P-values*
vanA	1.82	**0.033**
vanB	1.78	**0.003**
VanC-1	1.18	0.089
VanC-2	1.43	0.065
VanC-3	1.84	**0.003**
aac(6')-Ie-aph(2")-Ia	1.91	**0.005**
Tet(L)	1.09	0.064
Erm(B)	1.94	**0.008**
gelE	1.99	**0.002**
esp	2.76	**0.0005**
gyrA	1.87	**0.003**
slyA	1.79	**0.001**
cylA	1.72	**0.003**
cylB	1.76	**0.0002**
cylM	1.64	0.099
asa1	1.78	**0.003**
aggA	1.73	**0.003**
efaA	2.01	**0.005**
enlA	1.69	0.076

As can be viewed in Table 2, the resulting test shows no significant changing expression of viral genes of isolated *Enterococcus faecalis* between patient groups before taking Docetaxel drug and healthy donors (p>0.05).

In this study, 19 virulence genes of *Enterococcus faecalis* were examined. The 8 genes (*vanB, vanA, VanC-3, VanC-2, VanC-1, aac (6')-Ie-aph (2")-Ia, Tet(L), Erm(B))* of these 19 genes were related to the antibiotic resistance (vancomycin, gentamicin, tetracycline and erythromycin in respectively).Of the 11 virulence genes of mentioned bacteria (*gelE, esp, gyrA, slyA, cylA, cylB, cylM, asa1, aggA, efaA* and *enlA*) just 9 of them *(gelE, esp, gyrA, slyA, cylA, cylB, asa1, aggA, efaA*) showed a significant overexpression in patients' groups after chemotherapy(p<0.05). However, the analysis of obtaining data of the studied 2 genes (*cylM* and *enlA*) of isolated *Enterococcus feacalis* from the sufferers after and before chemotherapy show an overexpression of mentioned genes in the female group after taking the Docetaxel drug than another group, it was not statistically striking (p>0.05).

The analysis of 8 genes belonged to antibiotic resistance (*vanB, vanA, VanC-3, VanC-2, VanC-1, aac (6')-Ie-aph (2")-Ia, Tet(L), Erm(B))* shows that only 4 of 8 genes (*vanA, vanB, VanC-3, Erm(B), aac(6')-Ie-aph(2")-Ia*) have demonstrated a significant overexpression in the subjects group after chemotherapy than two another groups (p<0.05). Notwithstanding, there has been no statistically significant discrepancy between the expressed genes of healthy donors and females before taking the Docetaxel drug (p>0.05).

Table 4. Patients with antibiotic resistance

Genotype	*Cases*	*Antibiotic resistance*
vanA	10	Vancomycin 100 cases
vanB	4	
VanC-3	5	
vanA/vanB	27	
vanA/vanC-3	8	
vanC-3/vanB	10	
vanA/vanB/vanC-3	36	
aac(6')-Ie-aph(2")-Ia	75	Gentamicin 75 cases
Erm(B)	55	Erythromycin 55 cases

Of 400 treated sufferers, 230 patients showed antibiotic resistance: (100 cases were resistant to vancomycin, 55 subjects were resistant to erythromycin, and 75 cases were resistant to gentamicin) showing a significant correlation with overexpression of *vanB, VanC-3, Erm(B), aac (6')-Ie-aph (2")-Ia* genes, respectively (p<0.05) (Table 3 and 4). In the analysis of 400 patients after chemotherapy showed that *esp* gene expression significantly increased in 230 cases with antibiotic resistance than 170 sufferers after chemotherapy (p<0.05). However, another virulence gene has indicated over expression, it has not been significant (Table 5).

Table 5. P-values of *E. faecalis* microflora genes in patients with Antibiotic resistance (230) vs. patients without Antibiotic resistance (170) ($p<0.05$)

Gene	$(2^{-\Delta CTCT})$	*P-values*
vanA	1.79	**0.002**
vanB	1.65	**0.013**
VanC-1	1.13	0.32
VanC-2	1.04	0.26
VanC-3	1.72	**0.002**
aac(6')-Ie-aph(2")-Ia	1.79	**0.003**
Tet(L)	1.12	0.43
Erm(B)	1.82	**0.002**
gelE	1.55	1.43
esp	2.33	**0.0005**
gyrA	1.43	0.87
slyA	1.52	0.056
cylA	1.25	0.062
cylB	1.62	1.0052
cylM	1.01	1.002
asa1	1.32	0.061
aggA	1.49	1.005
efaA	1.63	1.002
enlA	1.04	0.09

Table 6. Comparing the analysis of data obtained after the end of the cycles of chemotherapy (1, 2, 3, 4) ($p<0.05$)

Name of the cycle	*vanA*	*vanB*	*VanC-1*	*VanC-2*	*VanC-3*	*aac(6')-Ie-aph(2")-Ia*	*Tet(L)*	
1/2	1.12	1.02	1.003	1.012	1.003	1.03	1.005	P-values
1/3	**0.0005**	**0.0005**	0.062	1.04	**0.004**	**0.0005**	1.06	P-values
1/4	**0.021**	**0.003**	0.099	0.075	**0.003**	**0.005**	0.087	P-values
2/3	**0.0005**	**0.0005**	0.066	0.098	**0.004**	**0.0005**	1.06	P-values
2/4	**0.021**	**0.003**	0.095	0.066	**0.003**	**0.005**	0.087	P-values
3/4	**0.031**	**0.031**	1.003	1.002	**0.045**	**0.002**	1.005	P-values
BP [a]/1	1.001	1.012	1.003	1.003	0.098	1.03	1.005	P-values
BP/2	1.001	1.012	1.003	1.003	0.098	1.03	1.005	P-values
BP/3	**0.0005**	**0.0005**	0.062	1.04	**0.004**	**0.0005**	1.06	P-values
BP/4	**0.033**	**0.003**	0.089	0.065	**0.003**	**0.005**	0.064	P-values
	Erm(B)	*gelE*	*esp*	*gyrA*	*slyA*	*cylA*	*cylB*	
1/2	1.02	0.99	0.12	1.03	1.003	1.005	0.98	P-values
1/3	**0.002**	**0.0005**	**0.0005**	**0.003**	**0.002**	**0.041**	**0.032**	P-values
1/4	**0.005**	**0.005**	**0.0005**	**0.003**	**0.002**	**0.003**	**0.0002**	P-values
2/3	**0.002**	**0.0005**	**0.0005**	**0.054**	**0.002**	**0.041**	**0.005**	P-values
2/4	**0.005**	**0.005**	**0.0005**	**0.065**	**0.002**	**0.003**	**0.0005**	P-values
3/4	**0.043**	**0.032**	**0.002**	**0.045**	**0.002**	**0.012**	**0.012**	P-values
BP [a]/1	1.02	0.99	**0.0005**	**0.002**	**0.002**	1.005	0.98	P-values
BP/2	1.02	0.99	**0.0005**	**0.002**	**0.002**	1.005	0.98	P-values
BP/3	**0.002**	**0.0005**	**0.0005**	**0.003**	**0.002**	**0.041**	**0.032**	P-values
BP/4	**0.008**	**0.002**	**0.0005**	**0.003**	**0.001**	**0.003**	**0.0002**	P-values

Table 6 continue

	asa1	*aggA*	*efaA*	*enlA*	*cylM*	
1/2	1.005	1.005	0.56	0.67	1.005	P-values
1/3	**0.032**	**0.002**	**0.001**	1.002	1.01	P-values
1/4	**0.02**	**0.003**	**0.005**	0.076	0.093	P-values
2/3	**0.032**	**0.002**	**0.001**	1.002	1.01	P-values
2/4	**0.02**	**0.003**	**0.005**	0.076	0.093	P-values
3/4	**0.02**	**0.045**	**0.02**	1.002	0.09	P-values
BP [a] */1*	1.005	1.005	0.56	0.98	1.005	P-values
BP/2	1.005	1.005	0.56	0.98	1.005	P-values
BP/3	**0.032**	**0.002**	**0.001**	1.002	1.01	P-values
BP/4	**0.003**	**0.003**	**0.005**	0.076	0.099	P-values

a: Patient before chemotherapy (BP)

In this study, patients were taken from faecal samples in chemotherapy courses. Comparing the analysis of data obtained after the end of the first cycle of chemotherapy and the second period of it showed no significant change. But there was a significant increase between the third cycle and the first and second courses. In the fourth cycle of chemotherapy, the level of change was significant.In the comparison of subjects before and after chemotherapy, in the first and second cycle only increases of *gryA*, *slyA* and *esp* were shown($p<0.05$) (Table 6).

DISCUSSION

The significant increase in breast cancer rate amongst Iranian females has been one of the important reason for the growth of the use of chemotherapeutic drugs (Docetaxel) to treat them in hospitals in Iran. Unfortunately, this group of the sufferer is continually at risk of miscellaneous types of infections (Kenmotsu and Tanigawara, 2015; Soha Sadeghi et al., 2018; Talebzade et al., 2018; Tayebe et al., 2017; Hoos, 2012).

The results of the inquiry showed a significant overexpression in fourteen out of nineteen investigated virulence gene (*vanA, vanB, VanC-3, aac(6')-Ie-aph(2")-Ia,Erm(B),gelE, esp, gyrA, slyA, cylA, cylB, asa1, aggA, efaA*) of the normal microbial flora of the body of patients after a period of chemotherapy with Docetaxel (Taxotere) drug compared to the other two classes ($P<0.05$). Therefore, the results may provide a support for the hypothesis that Docetaxel medicine may trigger to alter virulence gene expression of the normal microbial flora of the body. These findings are also consistent with several preceding studies on the side effects of cancer therapy methods on microorganism of the body. Talebzade and et al (2017) and Sadeghi and et al (2018) pointed out that patients with prostate cancer undergoing immunotherapy might suffer from a bacterial infection after ending therapy. They claimed that mentioned therapy method may have side effects causing growing the microflora pathogenicity risk in sufferers (Kenmotsu and Tanigawara, 2015; Tayebe et al., 2017). Also, Talebzade and et al (2018) carried out an investigation into side effects of chemotherapeutic drugs on vancomycin antibiotic resistance of isolated *Enterococcus feacalis* from colon cancer undergoing chemotherapy with 5-FU or capecitabine drugs. It has been shown that chemotherapycould significantly overexpress antibiotic resistance genes (*vanA* and *vanB*) in the group of the sufferers after therapy compared to the healthy subjects and patients prior to chemotherapy ($P<0.05$) (Talebzade et al., 2018).

Other studies have stated that radiotherapy and chemotherapy may swap numbers and diversity of the microflora of the body. The modifications could trigger the bacterial and viral infection in cancer patients undergoing those treatment methods (Nicolatou-Galitis et al., 2006; Fijlstra et al., 2015; Gafter-Gvili et al., 2012).

Antibiotic resistance has been a pivotal concern for the international community for more than four decades. Self-medication use and occasionally administration of antibiotics without performing laboratory diagnosis are a major cause of the development of antibiotic resistance. Addressing the issue of antibiotic resistance, more accurately examining genotype and resistant phenotype strain can help to understand resistance mechanisms and counteract the growing resistance of human pathogens. Enterococci are one of the most resistant bacteria against antibiotics. One of the main reasons for their role in nosocomial infection is the inherent resistance of this bacterium to several antibiotics (Parameswarappa et al., 2013; Kariyama et al., 2000).

Our result showed 230 participants with breast cancer after chemotherapy with Docetaxel drug encountering antibiotic resistance dilemma. Likewise, a significant

overexpression of *vanA, vanB, VanC-3,aac (6')-Ie-aph (2")-Ia*and*Erm (B)*genes were observed in isolated *Enterococcus feacalis* from these patients (P<0.05).This could prove that the chemotherapeutic medicines such as Docetaxel may have side effects on the normal microbial flora of the body and lead to antibiotic resistance.

Nevertheless, a question that needs to be answered is whether chemotherapeutic drugs could be responsible for altering virulence genes of the microflora of the body (such as antibiotic resistance genes) or not. To date, no research has been found the mechanisms of the effects of chemotherapy on microbial flora. Few researchers have addressed the issue. The paper particularly focuses on the side effects of Docetaxel drug on virulence genes of the microflora isolated from females with breast cancer undergoing mentioned drug. The normal microbial flora of the body serves as a barrier versus excess growth of opportunisticmicroorganisms and colonization of potentially pathogenic microorganisms. Some of the administration of antimicrobial agents, therapeutically such as chemotherapy, provokes perturbation in the ecological balance between the host and his microbial flora (Sullivan et al., 2001).

Over the past century, Over the past age, investigations which have focused on side effects of chemotherapy have been dramatically increased. Chemotherapy diminishes white blood cell production, which may trigger the growth of Gram-positive and Gram-negative bacteria. Antimicrobial agents cause disturbances in the balance of the microflora, and so the risk of emergence and spread of antibiotic-resistant strains increase.It is conceivable that the decreased number of white blood cells could set up a natural selection amongst microflora population and therefore, antibiotic resistance strains were selected to survive (Nowak et al., 2002). Ostensibly, preventive measures will be necessary to prevent infection.

Microbiological genetic research has been more of a concern for researchers over the past decades. One of the most important phenotypic characteristics of bacteria is the ability to grow and resist in an antibiotic-containing environment. One of the resistance mechanisms of bacteria against antibiotics is to receive resistance genes.However, there are other unknown mechanisms that cause antibiotic resistance (Kariyama et al., 2000). Qualitative genetic reviews such as mutations, SNPs, and quantitative genetic studies such as the expression of genes in resistant strains can help to understand these mechanisms.

One of the crucial objectives of this research was to improve and design a real-time PCR assay to enhance accuracy and quick identifying of E. faecalis' virulence genes and their antibiotic resistance genes, simultaneously. Scholars have identified various genes having roles in *E. faecalis* biofilm development, however, few researchers have addressed biofilm-associated antibiotic resistance genes. Thus, the biofilm resistance accurate mechanisms to antibiotics have not determined (Dale et al., 2017). Understanding particular genetic determinants, as well as comprehension similar putative mechanisms involving in biofilm antibiotic resistance, will be useful to prevent developing the infection.The findings of the study demonstrated that the expression of the *esp* gene significantly increased in 230 antibiotic resistance strain than 170 isolated *Enterococcus feacalis* from females after Docetaxel therapy (P<0.05) (Table5). Moreover, another 5 of the 9 virulence genes (*gelE, gyrA, slyA, aggA, enlA*) in the antibiotic-resistant group (230 subjects) have shown a significant overexpression than antibiotic sensitivity group (170 cases) (P<0.05). However, changes of expression of the *esp* gene were marginally higher than other genes.This could indicate the important role of biofilms in antibiotic resistance.

Another substantial aspect of this study was the sudden emergence of an increase in the expression of resistance to antibiotic genes in the post-chemotherapy group than the other two groups. This may be a confirmation of the side effects of Docetaxel drug on the microflora of the body to develop the infection. Esp is a giant surface protein, which delivers the purpose of colonization, support cell adherence, the escape of the immune system, and biofilm formation in *E.faecalis*.

The present scrutiny corroborates prior conclusions and provides further evidence that suggests assessing viral genes of the body's natural microflora (such as antibiotic-resistant genes) may help sufferers undergoing chemotherapy through prognosticate the onset of infection as well as recommending the suitable antibiotic therapy.

ACKNOWLEDGEMENTS

We appreciate Research Institute of Nikan Rooyesh Gene for its valuable cooperation in this study.

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