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The Effectiveness of Vaccines in Older Individuals Diagnosed with COVID-19: A Retrospective Cross-Sectional Study

COVID-19 Tanısı Alan Yaşlı Bireylerde Aşıların Etkinliği: Retrospektif Kesitsel Bir Çalışma

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ABSTRACT Objective: This study aimed to determine the effectiveness of vaccination status and vaccine types on the course and outcomes of the disease in the older individuals diagnosed with coronavirus disease-2019 (COVID-19). **Material and Methods:** The study included 1,258 individuals aged 65 years and older who were diagnosed with COVID-19 [polymerase chain reaction (PCR) test positive] between February and March 2022, and the study was conducted retrospectively. The vaccination status of the individuals, the types of vaccines administered to the individuals, and the number of vaccines were obtained from the Vaccine Tracking System. PCR results, hospitalization, and rates of death were obtained from the Public Health Management System. **Results:** Over 80 years of age was identified as a significant risk factor. In patients vaccinated with at least one dose of mRNA, the rate of intensive care unit treatment was 1%, and the rate of exitus was 0.2%. While 14% of individuals who had never been vaccinated were treated in the intensive care unit, all of these individuals became exitus. Among individuals vaccinated with at least 2 doses of inactivated vaccine, 6.4% were admitted to the intensive care unit, while 5% became exitus. It was determined that patients who received at least one dose of the mRNA vaccine were 93% protected from the need for intensive care and 99% protected from death. **Conclusion:** In terms of public health policies, appropriate vaccination, planning, and implementation of booster doses after vaccination are the most effective methods to protect older people from COVID-19.

Keywords: Aged; vaccination; COVID-19; inactivated vaccine; mRNA vaccine

ÖZET Amaç: Bu çalışmanın amacı, koronavirüs hastalığı-2019 [coronavirus disease-2019 (COVID-19)] tanısı almış yaşlı bireylerde aşılama durumları ve aşı çeşitlerinin hastalığın seyri ve sonuçları üzerindeki etkisini belirlemektir. **Gereç ve Yöntemler:** Çalışmaya Şubat-Mart 2022 tarihleri arasında COVID-19 [polimeraz zincir reaksiyonu (polymerase chain reaction "PCR") testi pozitif] tanısı konan 65 yaş ve üstü 1.258 birey dâhil edildi ve çalışma retrospektif olarak yapıldı. Bireylerin aşılanma durumları, bireylere uygulanan aşı türleri ve aşılanma sayıları Aşı Takip Sistemi'nden elde edildi. PCR sonuçları, hastaneye yatış ve ölüm oranları ise Halk Sağlığı Yönetim Sistemi'nden elde edildi. **Bulgular:** Seksen yaş üstü olmak önemli bir risk faktörü olarak belirlendi. En az bir doz mRNA ile aşılanan hastalarda yoğun bakımda tedavi görme oranı %1, eksitus oranı %0,2 idi. Hiç aşı yaptırmayan bireylerin %14'ü yoğun bakımda tedavi altına alınırken tamamı eksitus oldu. En az 2 doz inaktif aşı ile aşılanan bireylerin %6,4'ü yoğun bakıma yatarken, %5'i eksitus oldu. En az bir doz mRNA aşısı yapılan bireylerin, %93 oranında yoğun bakım ihtiyacından, %99 oranında ise ölümden korunduğu belirlendi. **Sonuç:** Halk sağlığı politikaları açısından uygun aşılama, planlama ve aşılama sonrası rapel dozların uygulanması yaşlı bireyleri COVID-19'dan korumada en etkili yöntemlerdir.

Anahtar Kelimeler: Yaşlı; aşılama; COVID-19; inaktive aşı; mRNA aşısı

The World Health Organization (WHO) reported an outbreak of acute lower respiratory tract infection in Wuhan, China, on December 31, 2019. The disease caused by the virus, called "severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2)," because it is a new type of coronavirus, was named coronavirus disease-2019 (COVID-19). SARS-CoV-2 continued to spread rapidly worldwide and was declared a pandemic by WHO on March 11, 2020. As of October 20, 2022, there were 623 million cases worldwide and more than 6.5 million deaths due to COVID-19.[1] In Türkiye, the first case was detected on March 10, 2020, and the first COVID-19-related death occurred on March 15, 2020.[2]

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The severity of the disease and poor prognosis in COVID-19 increases in direct proportion with age. It has been shown that the presence of comorbid diseases with old age also increases hospitalizations and deaths due to COVID-19.[3] According to a report by the US Centers for Disease Control and Prevention (CDC), older individuals aged 65 years and older have a 5 to 15 times higher risk of hospitalization compared to young adults aged 18-29 years. Eight out of ten deaths due to COVID-19 occure in people aged 65 years and older.[4] For this reason, it is very important in the management of the pandemic that especially the older people should be vaccinated to protect them from COVID-19 and recover quickly when they get sick.

Masks, social distancing, and isolation were the most important methods of protection against COVID-19 at the onset of the pandemic. With the production and use of vaccines, however, a significant milestone has been reached, particularly in the protection of people over 65. According to a study conducted by the CDC, full-dose vaccination reduced the hospitalization rate in older patients by 94%.[5] In the study of full dose and booster dose vaccine efficacy with BNT162b2 in >50 years old, it was reported that full dose vaccination was 96.9% protective against death and booster dose vaccination was 99.2% protective against death.[6]

Prevention of COVID-19 in elderly individuals aged 65 years and over, and rapid recovery if they catch it, constitute the most important part of the country's epidemic plans. This study aimed to determine the effectiveness of vaccination and vaccine types on the course and outcomes of the disease in the older people diagnosed with COVID-19.

MATERIAL AND METHODS

STUDY SAMPLE

The study was conducted retrospectively on October 1-20, 2022, in Çankırı province and its districts through the Health Information System data. The study included 1,258 individuals aged 65 years and older who were diagnosed with COVID-19 between February 1, 2022, and March 31, 2022. The average age was 73.98±7.14 years, while the average age of female was 74.2±7.28 years, and the average age of male was 73.8±6.98 years. 50.9% of the cases were female, and 49.1% were male. At the beginning of the pandemic in Türkiye, waves of alpha and delta variants were observed, and the Omicron variant was observed to be the predominant variant between February and March 2022.[7] Accordingly, the date range for sample selection was established. The study sample consisted of COVID-19 polymerase chain reaction (PCR) test-positive cases.

EXCLUSION CRITERIA

- Individuals under 65 years old.
- People who had coronavirus disease before February 1, 2022.
- Individuals who were hospitalized were admitted to intensive care and died due to a cause other than coronavirus disease.
- Patients receiving treatment with a computed tomography (CT) report compatible with COVID-19 but with a negative PCR test.

VACCINATION AND PCR DATA

The vaccination status of individuals was obtained from the Vaccine Tracking System (VTS), and PCR results and reasons for hospitalization and death were obtained from the Public Health Management System (PHMS). PCR-positive cases in which 14 days had not elapsed since the last vaccine dose were included in the study without counting the last vaccine dose, as it was considered that there was not enough time for neutralizing antibody formation.

Within the scope of the fight against the COVID-19 pandemic in Türkiye, vaccination started with healthcare workers on January 14, 2021, and the process continued with individuals over the age of 65.[8] Since the first inactivated full virion SARS-CoV-2 vaccine (CoronaVac; Sinovac Life Sciences, China) was available on these dates, vaccination started with the CoronaVac vaccine. With the acceleration of vaccine procurement efforts, the messenger ribonucleic acid (mRNA) vaccine BNT162b2 (BNT162b2; Pfizer-Biontech, United States-Germany) was offered to vaccine preferences in our country. With two different vaccine types and the use of booster doses

throughout the process, many vaccine groups with heterologous vaccination have been formed. Vaccinated individuals were grouped according to the number of inactive and mRNA doses (Table 1).

ETHICS

Prior to the study, approval was obtained from the Ministry of Health COVID-19 Scientific Research Evaluation Commission (date: February 07, 2022), Çankırı Karatekin University Ethics Committee (date: September 28, 2022, no: 27), and Çankırı Provincial Health Directorate Scientific Research Permission Commission (date: September 30, 2022). The research was conducted in accordance with the Helsinki Declaration.

STATISTICAL ANALYSIS

The data were recorded and statistically analyzed with IBM SPSS statistics 25 (International Business Machines Corporation, United States). The conformity of the quantitative data to normal distribution was evaluated with kurtosis and skewness values. Skewness value was found between -1.103 and 0.109; kurtosis value was found between -0.785 and -0.935. In the literature, a normal distribution is accepted if it is between -1.5 and +1.5.[9] Descriptive statistical methods are shown as percentages. Pearson chi-square analysis was used for the relationship between categorical variables. Statistical analyses were performed at a 95% confidence interval ($p<0.05$).

RESULTS

According to data from the PHMS, between February 1, 2022, and March 31, 2022, a total of 1,258 patients aged 65 and older were identified. 50.9% of the cases were female, the average age was 73.98±7.14 years. The highest number of positive cases was in the 65-69 age group. When the vaccination status of the patients from VTS was examined and divided into vaccine groups, it was observed that 50 patients (4%) had never been vaccinated, 161 patients (12.8%) did not receive booster dose vaccines after 2 doses of inactivated vaccine, and 598 patients (47.5%) included mRNA vaccine in their vaccine preferences. 151 patients (12%) were hospitalized and treated within the indication due to COVID-19, 52 patients (4.1%) needed intensive care treatment, and 39 patients (3.1%) became exitus due to COVID-19. 1,107 (88%) of PCR-positive patients aged 65 years and older did not require hospitalization and survived the disease mildly by following home isolation rules (Table 2).

When the need for intensive care and exitus rates of patients according to the age group were analyzed; 32 (11.3%) of 282 patients aged 80 years and over required intensive care treatment, while 20 (2%) of 976 patients under 80 years old received intensive care treatment ($p<0.001$). While 25 (78.1%) of 32 patients over 80 years of age who were admitted to the intensive care unit (ICU) became exitus, 14 (70%) of 20 patients under 80 years old admitted to the ICU became exitus. The need for intensive care and mortality rates increased with age, but there was no significant correlation between age and the recovery status of intensive care patients (Table 3).

When the need for intensive care and exitus rates were analyzed according to vaccination status, 6 (1%) of 598 patients who were vaccinated with at least 1

TABLE 1: Vaccine groups formed according to vaccine types.

Vaccine groups	Vaccination status
Unvaccinated group	Never been vaccinated
2 doses of inactivated vaccine group	CoronaVac-CoronaVac
3 doses of inactivated vaccine group	CoronaVac-CoronaVac-CoronaVac
4 doses of inactivated vaccine group	CoronaVac-CoronaVac-CoronaVac-CoronaVac
2 doses of inactivated-1 dose of mRNA vaccine	CoronaVac-CoronaVac-BNT162b2
2 doses of inactivated-2 doses of mRNA vaccine	CoronaVac-CoronaVac-BNT162b2-BNT162b2
2 doses of mRNA group	BNT162b2-BNT162b2

TABLE 2: Demographic characteristics, vaccination status, intensive care hospitalization and mortality rates of the patients.

	Number (n)	Percentage (%)
Gender		
Male	618	49.1
Female	640	50.9
Total	**1,258**	**100.0**
Age groups		
65-69	430	34.2
70-74	328	26.1
75-79	218	17.3
80-84	159	12.6
85-89	82	6.5
>90	41	3.3
Total	**1,258**	**100.0**
Age		
Average	73.98	
Standard deviation	7.136	
Minimum-maximum	65-98	
Median	72	
Vaccine groups		
Unvaccinated	50	4.0
2 doses of inactivated vaccine	161	12.8
3 doses of inactivated vaccine	289	23.0
4 doses of inactivated vaccine	160	12.7
2 doses of inactivated vaccine+1 dose of mRNA vaccine	298	23.7
2 doses of inactivated vaccine+2 doses of mRNA vaccine	263	20.9
2 doses of mRNA vaccine	37	2.9
Total	**1,258**	**100.0**
Admission to the care unit		
Number of patients admitted to caring units	151	12.0
Number of patients not admitted to care units	1,107	88.0
Total	**1,258**	**100.0**
Admission to ICU		
Patients admitted to ICUs	52	4.1
Patients not admitted to ICUs	1,206	95.9
Total	**1,258**	**100.0**
Last condition		
Patients who became exitus	39	3.1
Patients cured	1,219	96.9
Total	**1,258**	**100.0**

ICU: Intensive care unit.

dose of mRNA received treatment in the ICU, and 1 (0.2%) of them became exitus. While 14% of individuals who were never vaccinated received treatment in the ICU, all of them resulted in exitus. 12.4% of individuals vaccinated with 2 doses of inactivated vaccine were admitted to the ICU, while 11.2% became exitus. Of a total of 449 patients who received the booster dose of inactivated vaccine, 19 (4.2%) were treated in the ICU, while 13 (2.9%) became exitus (Table 3).

When the situation between gender and prognosis was analyzed; 31 (5%) of 618 male patients were admitted to the ICU, and 21 (3.4%) died, while 21 (3.3%) of 640 female patients were treated in the ICU and 18 (2.8%) died. While the need for intensive care was 1.51 times higher and death was 1.21 times higher in males than females, no statistically significant difference was found ($p<0.549$) (Table 3).

When the efficacy of the vaccine groups in postponing ICU admission and in protecting against death was examined in the study, it was observed that patients who received at least one dose of mRNA vaccine were 93% protected from ICU admission and 99% protected from death, while those who used the booster dose of inactivated vaccine were 70% protected from ICU admission and 79% protected from death. In the 2 doses of inactivated vaccine group, protection from intensive care was 11%, and protection from death was 20% (Table 4).

In the 2 doses of inactivated vaccine group, the mean duration after the last dose was 305 days (44 weeks), while in the 3 and 4 doses of inactivated vaccine groups, the mean duration after the last dose was 171 (24 weeks) and 48 (7 weeks) days, respectively. After 2 doses of inactivated vaccine, the mean duration after the last dose of vaccine was 182 days (26 weeks) in the group receiving 1 dose of mRNA booster vaccine and 66 days (9 weeks) in the group receiving 2 doses of mRNA booster vaccine (Table 5).

DISCUSSION

The results of the present study were discussed in the light of previous literature. Additionally, the effectiveness of the vaccines administered to the older individuals, the most risky population, in preventing intensive care admissions and deaths during the Omicron variant period was evaluated.

In the results of the study, important findings constituting the main themes were reached. The discussion was shaped around these findings.

TABLE 3: Need for intensive care treatment and exitus rates of patients by age group, vaccination status, and gender.

	Number (n)	Admission to ICU	Percentage (%)	p value	Exitus	Percentage (%)	p value
Age							
65-79	976	20	2.05	**0.000**	14	1.43	**0.000**
≥80	282	32	11.35		25	8.87	
Total	**1,258**	**52**	**4.13**		**39**	3.10	
Vaccine groups							
Unvaccinated	50	7	14.0[a]	**0.000**	7	14.0[c]	**0.000**
2 doses of inactivated vaccine	161	20	12.4[a]		18	11.2[c]	
3 doses of inactivated vaccine	289	12	4.2		8	2.8	
4 doses of inactivated vaccine	160	7	4.4		5	3.1	
2 doses of inactivated vaccine+1 dose of mRNA vaccine	298	5	1.7[b]		1	0.3[d]	
2 doses of inactivated vaccine+2 doses of mRNA vaccine	263	1	0.4[b]		0	0.0[d]	
2 doses of mRNA vaccine	37	0	0.0[b]		0	0.0[d]	
Total	**1,258**	**52**	**4.1**		**39**	**3.1**	
Gender							
Male	618	31	5.0	**0.122**	21	3.4	**0.549**
Female	640	21	3.3		18	2.8	
Total	**1,258**	**51**	**4.1**		**39**	**3.1**	

Pearson chi-square analysis was used, [a,b,c,d] Catagories with different letters are statisticaly significant, p<0.05 significant; ICU: Intensive care unit.

TABLE 4: Relative risk and vaccine efficacy in terms of intensive care need and exitus according to vaccine groups.

	Need for ICU Relative risk (RR)	Vaccine efficacy in terms of intensive care need (VE)		Exitus Relative risk (RR)	Vaccine efficacy in terms of exitus protection (VE)	
2 doses of inactivated vaccine	0.89	11%		0.80	20%	
3 doses of inactivated vaccine	0.30	70%	**70%**	0.20	80%	**79%**
4 doses of inactivated vaccine	0.31	69%		0.22	78%	
2 doses of inactivated vaccine+1 dose of mRNA vaccine	0.12	88%	**93%**	0.02	98%	**99%**
2 doses of inactivated vaccine+2 doses of mRNA vaccine	0.03	97%		0.00	100%	
2 doses of mRNA vaccine	0.00	100%		0.00	100%	

$VE = \frac{\text{Incidence unvaccinated} - \text{Incidence vaccinated}}{\text{Incidence unvaccinated}}$, $RR = \frac{\text{Incidence vaccinated}}{\text{Incidence unvaccinated}}$, $VE=1-RR$.

TABLE 5: Time elapsed after the last dose in the vaccine groups.

Time elapsed after the last dose	Mean	Median	Minimum	Maximum	SD
2 doses of inactivated vaccine	305	324	115	389	65
3 doses of inactivated vaccine	171	182	14	266	48
4 doses of inactivated vaccine	48	46	14	103	37
2 doses of inactivated vaccine+1 dose of mRNA vaccine	182	188	14	271	50
2 doses of inactivated vaccine+2 doses of mRNA vaccine	66	61	14	220	35
2 doses of mRNA vaccine	220	219	130	351	51

SD: Standart deviation.

One of the main findings of the current study is that the rates of hospitalization and death in the ICU are lower in vaccinated elderly patients than in patients who have never been vaccinated. In the current study, the effect of the vaccine in recovery from the disease was revealed. In current study, an efficacy of

70% in preventing ICU admission and 76% in preventing death for all vaccines was found. In a study conducted in Colombia in individuals aged 60 years and older, 61.6% in preventing hospitalization and 72.8% in preventing death were observed.[10] It is compatible with our study regardless of vaccine differences. According to the mentioned literature and the results of the current study; recovery is faster, hospitalization and death rates are lower in the elderly individuals who are vaccinated compared to those who do not.[10]

The second main finding of the current study is that the protective effect of the mRNA (BNT162b2) vaccine on recovery in older patients is extremely high compared to the inactivated vaccine. In older patients who were fully vaccinated with at least 1 dose of BNT162b2, vaccine efficacy was 93% in preventing the need for intensive care and 99% in protecting from death. The booster dose protected 70% from ICU admission and 79% from death in inactivated vaccine groups. When the previous literature is examined; in the study conducted by Arregocés-Castillo et al., BNT162b2 vaccinated individuals provided 83% protection from hospitalization and 94.8% protection from death; the CoronaVac vaccine provided 47.3% protection from hospitalization and 72.1% protection from death.[10] Mazagatos et al. found 88.4% protection against hospitalization and 97% protection against death in a study conducted in Spain in individuals aged 65 years and older who were fully vaccinated with the BNT162b2 vaccine.[11] In a study of nursing home residents in Catalonia, it was found protection 95% from hospitalization and 97% from death.[12] In a cohort study in Portugal conducted by Nunes et al., BNT162b2 vaccine efficacy in 18 million people aged 65 years and over was 59% in reducing the risk of hospitalization and 81% in reducing death.[13] In a study by Jara et al., full doses of inactivated vaccines were found to protect 89.2% from the need for intensive care and 86.5% from death in individuals aged 60 years and older.[14] In current study, the BNT162b2 vaccine showed the effectiveness of BNT162b2 vaccine in protecting from ICU hospitalization and death in older patients, in which the groups vaccinated with BNT162b2 were consistent with the literature. In the light of the current study results and previous literature, the protective efficacy of the mRNA (BNT162b2) vaccine was evaluated as high. The most important finding that the results of the study contribute to the field of public health is the fact that the mRNA vaccine is reliable in protecting the older people. Today, it is a fact that the side effects of vaccines are also discussed, and studies are needed on this. However, mRNA vaccine is effective and reassuring in prevention.

The third main finding of the current study is the time elapsed since the last vaccine administered. When the previous literature is examined; Lin et al. analyzed the efficacy of the BNT162b2 vaccine in preventing hospitalization and death based on the time elapsed after vaccination. At the end of the study, it was observed that the vaccine efficacy against hospitalization, which was 96.4% at the beginning, decreased to 90.5% at the end of 6 months.[15] Andrews et al. showed that in the study in which they tried to show BNT162b2 vaccine efficacy as time passed in the elderly over 65 years of age, protection from hospitalization decreased from 98% to 90.5% at the end of 20 weeks; protection from death decreased from 97.1% to 90.2%.[16] In a study, vaccine effect at 28-34 days post-vaccination against COVID-19 hospital admissions among those receiving of the vaccine BNT162b2 was 91%.[17] In current study, in the group that received 2 doses of inactivated and 2 doses of mRNA vaccine, the mean duration after the last dose was 66 days (9 weeks), which was in the period when neutralizing antibody levels were high and were consistent with other studies. The fact that the mean duration after 2 doses of inactivated vaccine was 305 days (44 weeks) and the rates of hospitalization in the ICU and mortality were similar with the unvaccinated group suggested that the serum neutralizing antibody level was no longer formed in these weeks in the inactivated vaccine. In addition, unlike other studies, the fact that current study was conducted in the Omicron variant period is one of the factors affecting the study. These results highlight how important it is to do booster doses in vaccinations.

The fourth main finding of the current study is the high efficacy of heterologous vaccinations. In the current study, inactivated and mRNA heterologous

vaccination groups showed higher vaccine efficacy in protection from both ICU admission and death compared to other studies were found. Heterologous vaccination was thought to increase the neutralizing antibody level better. In a study conducted by Pozzetto et al., with ChAdOx1-S-nCoV-19 and BNT162b2 vaccines to demonstrate the level of neutralizing antibodies, ChAd/BNT-vaccinated individuals exhibited 2.3-3.6 times higher serum neutralizing antibodies than the BNT/BNT homologous vaccination group.[18]

Another main finding of the current study is that being 80 years or older poses a great risk. In current study, 11.4% of patients aged 80 years and older required intensive care, and 8.9% died, regardless of vaccine groups. Although vaccine efficacy was negatively correlated with age regardless of the vaccine group, the BNT162b2-vaccinated group was less affected than the inactivated group. The increase in deaths with age is due to the presence of age-related comorbid diseases and a lack of neutralized antibody levels formed by the vaccine, according to Crooke et al. and other studies.[19,20]

Although not statistically significant, gender is also a finding that should be mentioned in the current study. In a study conducted by Nguyen et al., with 308,010 people, mortality in COVID-19 patients aged 65 years and over was found to be 1.33-1.54 times higher in men.[21] In a study conducted in Pakistan, it was observed that the mortality rate was higher in men aged 60 years and over, but it was not statistically significant.[22] In our study, although vaccination types and age averages were similar according to gender, men were found to be 1.51 times more under risk of ICU hospitalizations and 1.21 times more under risk of deaths, and it was found to be consistent with the literature.

STRENGTHS AND LIMITATIONS OF THE STUDY

The most important strength of our study is the size of the sample and the fact that it was conducted in individuals aged 65 years and over, the group who is most at risk of COVID-19 effect. Various vaccines against COVID-19 are used in many countries, and the heterologous vaccination and heterologous vaccine efficacy found in our study will shed light on the vaccination policy of other countries during the pandemic. However, the fact that the patients had comorbid diseases due to age and the post-vaccine antibody levels were not known are among the most important limiting factors of our study.

CONCLUSION

The study revealed that vaccination will be protective in the elderly in COVID-19, the protective effect of the mRNA (BNT162b2) vaccine is strong, the efficacy in mRNA is higher than inactivated vaccines, and the booster doses are important.

The older people play a crucial role in pandemic management as hospitalization and mortality rates increase with age in most countries. This is one of the most comprehensive studies in Türkiye demonstrating the efficacy of the COVID-19 vaccine in patients older than 65. In light of these data, especially in the protection of older individuals from COVID-19, appropriate vaccination, planning, and implementation of booster doses after vaccination is the most effective and efficient practice in the fight against COVID-19 in the older people was revealed. Current study results will be a guide in guiding the preventive public health policies of our country and other countries in the world is believed.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

All authors contributed equally while this study preparing.

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