

An Evaluation of Maternal Near-Miss Patient Profiles, the Prevalence, Treatment Approach, Outcomes, and Prognostic Factors: A Retrospective Study

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ABSTRACT Objective: The aim of this study was to reduce maternal death rates and contribute to the literature by evaluating maternal near-miss (MNM) profiles, the prevalence, treatment approach, outcomes, and prognostic factors. **Material and Methods:** A total of 217 MNM patients and 19 cases of maternal death were included in this study. The criteria of organ dysfunction, revised by the World Health Organization (WHO) in 2009, was accepted as the criterion for patients defined as MNM. According to WHO's criteria, the patients were classified in 4 groups. These groups were classified as hypertensive pregnancies, hemorrhagic diseases, placental abruption and disseminated intravascular coagulation and other systemic diseases, respectively. **Results:** The MNM incidence was 2.31 per 100 live births, and the maternal mortality incidence was 202.4 per 100,000 births. The mortality rate of patients transferred to our hospital because of insufficient intervention at another centre was found to be statistically significantly higher. A statistically significant difference was determined in the laboratory parameters between the MNM cases and patients with maternal mortality in Group 1, 2, and Group 3. The rate of blood and blood products transfusion given to MNM patients was statistically significantly higher in Group 3 than in Group 2. **Conclusion:** The laboratory parameters found to be significant in MNM and maternal mortality cases could have a negative effect on prognosis and could be of guidance in the prediction of mortality. For patients with an insufficient treatment at other centres, transport to suitable centres would reduce maternal mortality by enabling appropriate interventions.

Keywords: Maternal near-miss; maternal death; maternal near-miss criteria; World Health Organization

Improving maternal health has been accepted as an element showing the development level of a country. Among the millennium healthcare goals declared by the World Health Organization (WHO), decreasing maternal mortality and improving maternal health are priority targets.

According to the WHO, patients who survive after developed life-threatening obstetric complications during pregnancy, birth, or in the postnatal period up to day 42 are defined as maternal near-miss (MNM).^{1,2} Maternal mortality is defined as death occurring during pregnancy or within the postnatal pe-

riod up to day 42 because of a disease associated with or exacerbated by the pregnancy, regardless of the duration and localisation of the pregnancy. This definition does not include deaths that occur coincidentally or as the result of an accident.^{3,4}

Maternal mortality rates are an extremely important measure of the level of health of a country. Moreover, maternal health is used to monitor the general quality of reproductive healthcare services and the progression of countries towards the international development targets. Relative to the maternal mortality rates, the MNM rates are higher in low- and

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middle-income countries than in high-income countries. Following the WHO recommendations for priority interventions in high-income countries with low maternal mortality rates and after starting to examine system deficiencies, researchers in many high-income countries have concentrated on MNM rather than maternal mortality.

Pregnancy-related hypertensive and haemorrhagic diseases, placental abruption and disseminated intravascular coagulation (DIC), and some systemic diseases (stroke, sepsis, shock, cardiac arrest, and respiratory system diseases) are of great importance to the aetiology of MNM. As the number of MNM cases is greater than the number of maternal deaths, there has been increased attention on the evaluation of these patient profiles to help reduce maternal mortality.^{1,2} Clarification of factors that cause fatal outcomes can be helpful and will provide crucial information that could improve maternal health.⁵ Over the years, several criteria had been suggested to define MNM.⁶ Due to the differences among these criteria, in 2009, the WHO proposed standardised descriptive criteria for MNM based on organ dysfunction; these criteria can be applied in all types of healthcare centres.⁷

The aim of this study was to examine maternal deaths and MNM patients meeting the criteria accepted by the WHO in 2009, and to determine the factors affecting prognosis by comparing the prevalence, treatment approach, and outcomes of the maternal deaths and MNM cases.

MATERIAL AND METHODS

This retrospective study included patients who gave birth in the Gynaecology and Obstetrics Clinic of Dicle University Medical Faculty between January 2013 and December 2017, or were referred to our hospital after the birth. The Ethics Committee of Dicle University Medical Faculty approved this study (date: June 06, 2018, no: 22). All procedures were performed according to the Declaration of Helsinki.

Patients were considered to be MNM cases if they met the criteria of organ dysfunction, as revised in 2009 by the WHO.⁷ All other patients were excluded.

The following information was collected for each included patient: age, gravida, parity, abortus, number of living children, gestational week, whether antenatal follow-up was at our hospital or elsewhere, gynaecological and obstetric history, mode of delivery, laboratory parameters (complete blood count, biochemistry, and coagulation parameters), type and number of transfusions, surgical interventions performed in our hospital and/or previously, complications that developed after hospital admission, and length of intensive care unit (ICU) stay. The estimated transfer time of patients transferred to our hospital after the birth was recorded according to the distance from our clinic. The data were retrieved from the hospital's archived records and the electronic archive database, including causes of death and complications resulting in maternal mortality.

The included patients were separated into four groups: hypertensive pregnancies (Group 1), haemorrhagic diseases (Group 2), placental abruption and DIC (Group 3), and other systemic diseases (Group 4). Group 1 included patients diagnosed with HELLP (hemolysis, elevated liver enzymes, low platelet) syndrome, eclampsia, or pre-eclampsia with severe characteristics. Group 2 included patients with postpartum haemorrhage, placental invasion anomalies, and uterine rupture. Group 3 included patients who developed placental abruption and DIC for obstetric reasons. Group 4 included patients diagnosed with pulmonary oedema, sepsis, shock, cardiac arrest, and systemic lupus erythematosus.

During the follow-up of the patients, the lowest and highest laboratory values were recorded for the complete blood count [hemoglobin, hematocrit, platelet (Plt), white blood cells (WBC), mean platelet volume], biochemistry [alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), urea, creatinine (Cr), total bilirubin], and coagulation parameters [international normalized ratio (INR), activated partial thromboplastin time (aPTT), partial thromboplastin time (PTT), fibrinogen, D-dimer]. The number of blood and blood product transfusions administered to each patient was recorded in units. The patients were assigned to one of the groups based on the available laboratory values and findings. As these patients

present a complicated clinical course and meet almost all the MNM diagnostic criteria, the group assignment was based on whichever criterion the patient met first. Within each group, the patients were defined as MNM or maternal mortality cases.

STATISTICAL ANALYSIS

The data were analysed with SPSS Statistics version 22 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to determine whether the data followed a normal distribution. The results are presented as the mean±standard deviation (SD) or the number (n) and percentage (%). Numerical data were analysed with the Student's t-test (if normally distributed) or the Mann-Whitney U test (if not normally distributed). Categorical data were analysed with the chi-square test. A p value <0.05 was accepted as statistically significant in all the tests.

RESULTS

Throughout the study period, 9,386 births occurred in our clinic, of which there were 217 patients who met the MNM criteria; 19 of these patients died and met the definition of maternal mortality. The MNM incidence was 2.31 per 100 births, and the maternal mortality incidence was 202.4 per 100,000 births.

The MNM criterion that was met first most often was ≥ 5 units red blood cells (RBC) replacement (73 cases, 33.6%), followed by hysterectomy performed

due to haemorrhage and infection (58 cases, 26.7%) (Table 1).

The mode of delivery was by the normal vaginal route in 35 cases (16.1%) and by caesarean section in 181 cases (83.4%); hysterotomy was performed in 1 patient (0.5%). Table 2 presents the places of residence of the MNM and maternal mortality cases, the places of first presentation, the surgical interventions performed in other centres, and the surgical interventions performed in our clinic. The mean length of ICU stay was 3.14 days for the MNM cases and 7.05 days for the maternal mortality cases. Overall, 100 cases (46.10%) required the ICU; 18 of the 19 maternal mortality cases (94.7%) required the ICU. Morbidity occurred in 55 cases (25.4%). For the maternal mortality cases, death was due to acute kidney failure, sepsis, respiratory failure, cardiac arrest associated with DIC and acute respiratory distress syndrome, or sudden cardiac arrest (Table 2).

Table 3 shows the demographic data and laboratory parameters for the MNM and maternal mortality cases in each group. For Group 1, the AST, ALT, LDH, INR, PTT, and D-dimer values were significantly higher, and the fibrinogen values were significantly lower in the maternal mortality cases compared with the MNM cases ($p < 0.05$). For Group 2, the Plt values were significantly lower and the WBC, AST, ALT, LDH, urea, Cr, INR, PTT, aPTT and D-dimer values were significantly higher in the maternal mortality cases compared with the MNM

TABLE 1: Evaluations of the maternal near-miss criteria according to the groups.

Criteria/Groups	Group-1	Group-2	Group-3	Group-4	Total
	hypertensive diseases	hemorrhagic diseases	detachment and DIC	other systemic conditions	
Cr \geq 3.5 mg/dL	6 (100%)	0	0	0	6 (100%)
Plt<50,000	48 (84.2%)	1 (1.8%)	3 (5.3%)	5 (8.8%)	57 (100%)
Hysterectomy performed because of hemorrhage and infection	1 (1.7%)	53 (91.4%)	4 (6.9%)	0	58 (100%)
≥ 5 units RBC replacement	1 (1.4%)	57 (78.1%)	15 (20.5%)	0	73 (100%)
Intubation for longer than 60 mins not related to anaesthesia	12 (80.0%)	1 (6.7%)	0	2 (13.3%)	15 (100%)
CPR	0	1 (33.3%)	1 (33.3%)	1 (33.3%)	3 (100%)
Shock	0	0	0	1 (100%)	1 (100%)
Stroke	4 (100%)	0	0	0	4 (100%)
Total	72 (33.2%)	113 (52.1%)	23 (10.6%)	9 (4.1%)	217 (100%)

Cr: Creatinine; Plt: Platelet; RBC: Red blood cells; CPR: Cardiopulmonary resuscitation; DIC: Disseminated intravascular coagulation.

TABLE 2: Evaluation of the general data of the MNM and maternal death patients.

		MNM n=217 (%)	Maternal death n=19 (%)
Place of residence	Diyarbakır	95 (43.8)	9 (47.4)
	Other	122 (56.2)	10 (52.6)
Place of first presentation	Dicle University	60 (27.6)	3 (15.8)
	Another healthcare institution in Diyarbakır	35 (16.1)	6 (31.6)
	Another province	122 (56.2)	10 (52.6)
Surgical intervention performed in another centre	None	124 (57.1)	5 (26.3)
	Normal vaginal birth	21 (9.7)	5 (26.3)
	Caesarean section birth	42 (19.4)	6 (31.6)
	Other	30 (13.8)	3 (15.8)
Surgical intervention performed in our clinic	None	67 (30.9)	10 (52.6)
	Caesarean section birth	74 (34.1)	2 (10.5)
	Normal vaginal birth	4 (1.8)	1 (5.3)
	Hysterectomy after caesarean	28 (12.9)	1 (5.3)
	Other	45 (20.3)	5 (26.3)
Distance from our clinic -transfer time (hours)		2.43±1.64	1.84±1.5
Intensive care unit requirement	Yes	100 (46.10)	18 (94.7)
	No	117 (53.90)	1 (5.3)
Morbidity developing after hospital admission	None	162 (74.6)	0 (0)
	ARF	18 (8.2)	2 (10.5)
	Sepsis	0 (0)	1 (5.2)
	Cardiac arrest	2 (0.9)	7 (36.8)
	Respiratory failure	4 (1.8)	4 (21)
	DIC	9 (4.1)	4 (21)
	Other	22 (10.1)	1 (5.2)

MNM: Maternal near-miss; ARF: Acute renal failure; DIC: Disseminated intravascular coagulation.

cases ($p < 0.05$). For Group 3, the AST, ALT, and LDH values were significantly higher in the maternal mortality cases compared with the MNM cases ($p < 0.05$). The Plt, WBC, and fibrinogen values were lower, and the urea, INR, PTT, aPTT, and D-dimer were higher in the maternal mortality cases compared with the MNM cases, but the differences were not significant ($p > 0.05$). For Group 4, the AST, ALT, LDH, urea, Cr, INR, aPTT and D-dimer values were higher in the maternal mortality cases compared with the MNM cases, but as the number of patients was low, the differences were not significant ($p > 0.05$). The PTZ value was significantly higher in the maternal mortality cases compared with the MNM cases ($p < 0.05$).

The mean number of fresh frozen plasma, random thrombocyte, haemocompent, and fresh full blood product transfusions were significantly higher in the Group 3 MNM cases compared with the Group 2 MNM cases ($p < 0.05$) (Table 4).

Finally, we evaluated whether there was a difference in the mortality rate for patients who were treated at another centre and then transferred to our tertiary-care institution. The mortality rate of patients who had undergone an intervention at another centre before being transferred was significantly higher than the patients who were only treated at our institution ($p < 0.05$) (Table 5).

DISCUSSION

The incidence of MNM in the present study (2.31%) is higher than in previous studies in high-income countries that used the same WHO criteria, namely 0.48% in Australia and 0.36% in Ireland. The incidence in studies in low-income countries, again using the same WHO criteria, has been reported to be 19.8% in Nigeria, 1.21% in Egypt, 0.4% in China, and 3.49% in Peru.⁸ The higher MNM incidence in our clinic compared with most countries and regions

TABLE 3: The demographic data and laboratory parameters (complete blood count, biochemistry, coagulation values) of the maternal near-miss cases in Groups 1, 2, 3, and 4.

	Group-1 n=72 X̄±SD	Group-2 n=113 X̄±SD	Group-3 n=23 X̄±SD	Group-4 n=9 X̄±SD
Age (years)	29.81±7.78	32.58±6.86	32.39±7.56	29.33±7.29
Gravida	3.89±3.05	4.85±2.70	5.39±2.31	6.11±4.40
Parity	2.49±2.19	3.82±2.29	4.43±2.55	3.89±3.06
Abortus	0.64±1.32	0.47±0.94	0.52±0.94	1.56±2.60
Number of living children	2.29±2.13	3.58±2.12	3.91±2.31	3.22±1.98
Hct (%)	31.14±7.00	23.71±5.66	22.88±6.13	28.67±3.26
Hgb (g/dL)	11.23±7.94	7.91±1.94	7.56±2.02	9.37±1.16
Plt (K/uL)	76.817±77.483	143.082±70.980	92.630±57.822	114.005±132.235
MPV (fL)	10.27±2.81	8.20±1.57	8.82±2.45	8.13±1.25
WBC (K/uL)	14.155±6.960	14.110±6.017	15.715±7.782	9192±5286
AST	282.22±377.86	28.83±37.37	53.39±69.33	57.44±24.19
ALT	167.65±245.72	14.58±17.89	26.61±43.41	26.67±18.43
LDH	992.79±608.520	396.00±228.04	568.78±432.93	471.78±144.61
Urea	47.17±49.92	19.52±12.04	40.78±26.90	33.89±31.29
Creatinine	1.45±1.75	0.66±0.35	1.22±1.13	1.07±1.17
Total bilirubin	1.98±3.27	1.13±1.55	1.34±1.24	1.66±1.97
INR	1.07±0.29	1.18±0.43	1.24±0.32	1.16±0.38
aPTT	32.42±12.47	33.75±10.53	35.34±13.30	33.33±10.95
PTZ	13.23±3.52	14.50±4.24	15.21±3.69	14.34±4.96
Fibrinogen	328.53±124.97	255.45±131.66	158.12±94.58	292.89±99.01
D-Dimer	10.55±15.34	13.89±23.98	32.59±41.03	14.00±12.91

Hct: Hematocrit; Hgb: Hemoglobin; Plt: Platelet; MPV: Mean platelet volume; WBC: White blood cells; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase; LDH: Lactate dehydrogenase; INR: International normalized ratio; aPTT: activated partial thromboplastin time; PTT: Partial thromboplastin time; SD: Standard deviation; Data are presented as mean±SD values.

TABLE 4: Evaluation of the blood and blood products transfusions administered to the Group 2 and Group 3 maternal near-miss cases.

	Group-2 X̄±SD	Group-3 X̄±SD	p value
ERS	5.26±2.89	5.35±2.90	0.827
FFP	3.41±2.80	5.87±5.42	0.019
Apheresis	0.13±0.50	0.48±1.08	0.060
Random thrombocytes	0.45±2.09	0.83±1.80	0.023
Hemocompetent	0.39±0.76	0.61±0.72	0.050
Fresh blood	0.37±0.91	1.13±1.57	0.011

ERS: Erythrocyte suspension; FFP: Fresh frozen plasma; Data are presented as mean±SD, frequency, percentage. Mann-Whitney U test; SD: Standard deviation. p<0.05 is statistically significant.

TABLE 5: Comparisons of mortality and the status of having undergone intervention at another centre of the MNM and maternal death cases.

	Maternal death	MNM	Total	p value
Intervention performed	No 5 (3.9%)	124 (96.1%)	129 (100%)	
at another centre	Yes 14 (13.1%)	93 (86.9%)	107 (100%)	0.010
Total	19 (8.1%)	217 (91.9%)	236 (100%)	

MNM: Maternal near-miss; Data are presented as mean±standard deviation, frequency, percentage; Mann-Whitney U test. p<0.05 is statistically significant.

can be attributed to our hospital being one of the few tertiary-level centres in the region, providing prenatal and neonatal care services and intensive care

services for every branch. Our centre can provide a multidisciplinary treatment approach for morbidities that can result in maternal death; therefore, high-risk and complicated pregnancies are transferred to our institution. In a previous study in Türkiye, 84 MNM cases met different criteria in a 15-month period and the MNM rate was 3.05%.⁹

In the current study, the maternal mortality rate was 202.4 per 100,000 births. Although this rate is below the global average, it is much higher than the rates for high-income countries. We think this high rate is due to the referral to our tertiary-level centre of patients in the region with a high risk of mortality. Yalınkaya et al. examined exitus in patients in our centre between 2001 and 2005 and reported a maternal mortality rate of 1,100 per 100,000 live births.¹⁰ Hence, the maternal mortality rate has decreased approximately 5-fold in 12 years. Developments in medical facilities, the provision of care via a multidisciplinary approach by an experienced team, and the recent important development of starting antenatal care at the lowest level of healthcare institutions have contributed to reduce this rate. In a study in a tertiary-level centre in Türkiye, Şimşek et al. reported a maternal mortality rate of 185 per 100,000 live births, lower but still close to the value we determined at our clinic.⁹

The most common aetiology of MNM in the current study was haemorrhagic diseases (52.1%) followed by hypertensive diseases (33.2%). These findings are consistent with the literature. When considering global data, these aetiologies emerge in both low- and high-income countries.⁸

Haemorrhagic and hypertensive diseases are thought to be the primary causes of MNM due to a delay in the diagnosis of the conditions, delayed management of complications, and late transfer to appropriate centres for treatment. In our study, the most common reasons for maternal mortality were postpartum haemorrhage and sepsis (21% each). Nakimuli et al. reported that the most common cause of MNM is pre-eclampsia (7%), followed by postpartum haemorrhage (6.7%) and uterine rupture (3.8%).¹¹ Maternal mortality was seen most often in the cases with uterine rupture (17.9%), followed by eclampsia (17.8%). In the current study, our centre was the place of first presentation for only 27.6% of the MNM cases and for 15.8% of the maternal mortality cases. Liyew et al. reported 88.2% of MNM cases were referred from another centre, and Nakimuli et al. stated that 28.4% of MNM cases and 12.3% of maternal mortality cases were referrals.^{11,12} The differences in the rates of transferred patients are

likely related to the medical facilities and capabilities of the centre to which the patient first presented.

We found that the diagnostic criterion for MNM that the patients met first most often was ≥ 5 units RBC replacement (33.6%), followed by hysterectomy due to haemorrhage and infection (26.7%) and platelet count $< 50,000$ (26.3%). Kiruja et al. reported neurological dysfunction (stroke, etc.) in 35.8% of MNM cases, cardiovascular dysfunction (cardiac arrest, cardiopulmonary resuscitation etc) in 10% of cases, and ≥ 5 units RBC replacement administered in 35.8% of cases.¹³ As the most common cause of MNM is known to be hypertensive and haemorrhagic diseases, attention must be paid to these patients with respect to the associated neurological and cardiological complications that can develop. Based on our analysis, the presence of these criteria could worsen the prognosis and potentially lead to death. However, this issue required additional prospective studies with more patients.

Laboratory values that differ significantly between MNM and maternal mortality cases have an important role in guiding the prognosis. Therefore, the laboratory parameters of these patients must be evaluated carefully, and additional precautions should be taken when there is a condition that negatively affects the prognosis (dialysis, admission to the ICU, intubation, blood and blood product replacement, etc.). Adamu et al. reported that the most frequent morbidities were neurological dysfunction (stroke, etc.; 52.4%), respiratory dysfunction (28.5%), and kidney dysfunction (15.8%).¹⁴ Although morbidity rates differ by region, the same morbidities are usually seen. Hence, they should be considered with respect to precautions, interventions, and treatment to reduce mortality.

When we examined the transfusions applied to the MNM and maternal mortality cases, we found that other than erythrocyte transfusions, there were more transfusions in the maternal mortality cases. This difference is likely due to a more severe condition in these patients and that a hyperacute and more aggressive approach was taken.

We found that as the length of ICU stay increased, the probability of mortality increased and the

prognosis could worsen. Almost all of the maternal mortality cases (18 or 19, 94.7%) died in the ICU. Therefore, when a potentially life-threatening condition develops, patients must be transferred to a centre that can offer intensive care via a multidisciplinary approach that addresses the patient's morbidities. This approach could lead to better outcomes and reduce mortality.

The rate of peripartum hysterectomy performed in MNM cases was 0.63%, higher than the rate of 0.32% reported in a previous study in Türkiye.⁹ In another study in a Turkish tertiary-level centre, Coskun et al. found that the rate of peripartum hysterectomy was 0.60%, very similar to our study. Evsen et al. conducted a study in our clinic between 2006 and 2010 and reported that in the MNM group, 68.3% of patients underwent peripartum hysterectomy and 50.7% showed placental invasion anomalies.^{15,16} While uterus-sparing surgery is performed routinely in patients with placental invasion anomalies admitted electively in our clinic, peripartum hysterectomy is performed more often in MNM cases. The reason for this high rate is thought to be due to loss of haemodynamic stability during transfer of these patients following an emergency intervention at another centre: time is lost, and haemostasis problems occur in patients who have to be transported over a long distance.

We found a significantly higher mortality rate for patients who had undergone an intervention in another centre prior to transfer to our institution. Once a patient has been diagnosed with a high-risk pregnancy, they should be referred to an appropriate multidisciplinary centre so that interventions can be performed in an appropriate environment. Interventions performed by inexperienced teams in unsuitable conditions will likely increase mortality; preventable causes of death can be overcome with regular antenatal care. However, when there are life-threatening emergencies, the decision for intervention must not be delayed: it should be made by reviewing the benefit-to-harm ratio.

The mean time it took the MNM cases to arrive at our clinic was 2.43 hours. The three-delays model is used in a global context to investigate and under-

stand the social, cultural, and medical events that contribute to maternal mortality.¹⁷ These three delays are a delay in deciding to seek medical service, a delay experienced in reaching the service, and a delay in receiving sufficient care despite having reached a healthcare institution. The mean time of 2.43 hours in this study is a long time for a high-risk pregnancy, and a reduction in this time might reduce mortality. This issue should be evaluated in larger prospective studies.

The strengths of our study are that it was conducted in a tertiary-level hospital that serves a large region and accepts high-risk patients, the patients were all of the same ethnicity, and many factors other than the MNM and maternal mortality rates were evaluated. However, the limitations are the retrospective design and the absence of a control group. Another limitation of our study is that the patients were followed by different doctors in our clinic.

CONCLUSION

We should recommend that pregnant women who are at risk for hemorrhagic disease and hypertensive disease, which are the most common in the etiology of MNM, should be identified in the early stages of pregnancy and their pregnancies follow-up and birth should take place in tertiary hospitals. We think that MNM and maternal mortality rates can be reduced by ensuring careful follow-up of patients whose laboratory parameters are not within normal limits. Transfer of patients with high risk of MNM and maternal death to tertiary hospitals should be facilitated so that their follow-up and treatment can be carried out as soon as possible.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or mem-

bers of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Gamze Akin Evsen, Mehmet Siddik Evsen; **Design:** Gamze Akin Evsen, Mehmet Siddik Evsen, Reyhan Gündüz, Mehmet Sait İçen; **Control/Supervision:** Gamze Akin Evsen,

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