

# A spectrum of severity and prevalence of malignant hyperthermia in anesthetized patients with inhalational anesthetic

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<sup>1-2</sup> Write-up and Data Collection

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<sup>5</sup> Conceptualize the study, final editing

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## A B S T R A C T

**Introduction:** Malignant hyperthermia (MH) or hyperpyrexia is a pharmacogenetic syndrome of skeletal muscles caused by volatile anesthetics such as halothane and depolarized muscle relaxant suxamethonium. The prevalence of MH in Islamabad has not been explored.

**Methodology:** This was a retrospective study on the severity and prevalence of MH in anesthetized patients with inhalational anesthetics. Clinical data from the previous years, i.e. from June 2020 to June 2021, from eight tertiary care hospitals in Islamabad was collected.

**Results:** Out of 40,900 patients discharged from these hospitals under general anesthesia, only 07 patients were diagnosed with MH due to anesthesia. MH is associated with gender; in our study, more incidence was observed in males than females. Of the seven patients with MH, four (57.14%) were males, and three (42.86%) were females. The prevalence rate of MH was 0.018% due to anesthesia in surgical patients which is approximately 1 per 5842 cases.

**Conclusion:** This research study concluded that the prevalence rate of MH in Islamabad is 0.018%. The prevalence rate for males is slightly higher than for females. According to this statement, the total number of male patients who got MH was four, and females were three out of 40900 surgical cases under general anesthesia in a specific year of duration. The prevalence of MH due to anesthesia in surgical patients treated in Islamabad hospitals is approximately 1 per 5842 cases. MH risk in males is significantly higher than in females.

**Keywords:** Anesthesia, Inhalation anesthetics, Malignant hyperthermia

## Introduction

Anesthesia is the state of controlled change or temporary loss of sensation for medical purposes. The patient becomes unconscious, either entirely or partially. It might incorporate a few or all of the absence of pain (help from or counteraction of agony), loss of motion (muscle unwinding), amnesia (loss of memory), and obviousness.<sup>1</sup> Anesthesia aims to achieve the point required for surgical

procedures with at least risk for the patient. Anesthesia is generally used for surgical procedures.<sup>2</sup>

General anesthesia is a therapeutically actuated trance-like state with loss of defensive reflexes because of the organization of at least one available sedative specialist. It is completed to permit operations that would somehow or another be grievously excruciating for the

patient or where the idea of the basic technique blocks the patient from being conscious.<sup>3</sup>

Anesthesia is administered by various routes, e.g., inhalational, injection (Intramuscular, Intravenous, or subcutaneous), oral, and rectal. General anesthetics are induced either inhalational or intravenous. Intravenous is faster than inhalation, taking about 10-20 seconds to cause total unconscious. Some anesthetic induction agents are propofol, ketamine, thiopental, etomidate, and methohexital.<sup>4</sup> Regional anesthesia should not be applied to surgical procedures needing muscle relaxants and analgesia. Such technique also should not be used for general anesthesia involving abdomen, thoracic, shoulder, neuro, cardiac, head and neck surgery.

However, anesthesia risks are generally associated, e.g., obstructive sleep apnea, where the patient stops breathing while sleeping; seizures; existing cardiac, renal, or lung diseases; hypertension; alcoholism; history of reactions to anesthesia and MH. The MH is the most lethal risk factor of general anesthesia.<sup>6</sup> It is a genetic disorder of skeletal muscle that is caused by certain drugs used for anesthesia (e.g., isoflurane, sevoflurane, halothane, Desflurane, Enflurane) and depolarizing muscle relaxants (e.g., suxamethonium).<sup>6, 7</sup> MH is manifested by hyper digestion caused by calcium entry from the sarcoplasm reticulum, high oxygen consumption, and unexplained CO<sub>2</sub> expansion that doesn't diminish with expanding minute ventilation, tachycardia, hyperthermia, and respiratory and metabolic acidosis.

Different indications of MH might cause intravascular coagulation, heart arrhythmias, hyperkalemia, hypophosphatemia, hypocalcemia, and marbled skin.<sup>6, 7</sup> Other symptoms include increased end-tidal carbon dioxide, skeletal muscle rigidity, muscle spasm, tachycardia and sweating.<sup>8, 9</sup> The incidence of MH during general anesthesia is 1:10,000 up to 1: 250,000. While in the case of females, the incidence of MH is less common than in young male patients within the age limit of under 30. In contrast, MH is less common in ages above 30.<sup>10</sup> This research aims to identify the range of severity and prevalence of MH in patients anesthetized with an inhalational anesthetic agent. According to a survey conducted in 2008 in Japan, a total of 187,097 cases were performed under general anesthesia in Japan in one month. The survey included a total number of cases served

1,238,171 under general anesthesia in 18 months. The result showed that the prevalence of MH in Japan's population (13.7 per million) in 2006-2008 was similar to the previous year (16.6 per million).<sup>11</sup> According to the North American report of 2007 – 2012, the cases of MH fatality rate have increased by up to 10%, and morbidity and mortality of MH when the administration of dantrolene is delayed. The administration of succinylcholine without volatile anesthetics resulted in 24 MH events. One patient died, while fourteen suffered severe complications.<sup>12-14</sup> MH is an intriguing issue.

MH in inpatient settings has emerged as an exciting issue, and it has been reported from managerial information and records that MH's defenselessness is a compelling issue. Revealed pervasiveness of MH analysis in examinations utilizing emergency clinic release records from administrative information goes from 0.18 per 100,000 (95% certainty span (CI), 0.12-0.25) in wandering a medical procedure place patient to 0.96 (95% CI, 0.75-1.41) in careful inpatients.<sup>6, 15</sup>

The lowest recurrence of MH emergencies and the expense of loading dantrolene have led to worry about the money-saving advantage of the suggestion of the MH Association of the United States (MHAUS) that dantrolene be made promptly accessible (for organizations inside 10 min) in working room regions, particularly in offices with low usage of general anesthesia and setting off specialists like maternity units.<sup>16</sup> MH Association of the United States is a patient security and support association, and its suggestions are utilized by certifying offices, like the Joint Commission, to evaluate readiness for an MH occasion during review visits. Notwithstanding, no review has explicitly inspected the commonness of MH powerlessness in obstetric patients.<sup>14</sup>

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## Methodology

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This research is a retrospective study in which we aimed to determine the severity and prevalence of MH in anesthetized patients with inhalational anesthetics. The study population for this research included all surgical procedures under general anesthesia visiting eight tertiary care hospitals of Rawalpindi and Islamabad. Data was collected after approval from the Ethics and Research Committee of Bashir Institute of Health Sciences Islamabad and respective private hospitals from where

data was collected. A–validated questionnaire was used to collect data, and all the surgical procedures under general anesthesia were observed/recorded by visiting eight tertiary care hospitals in Rawalpindi and Islamabad. The study was conducted from September to December 2021. The sample size for this research was 40900.

The nonprobability convenience sampling method was used for data collection. Data were analyzed through SPSS software version 22. All surgical procedures under general anesthesia were included in this research study. Patients under ten years and those who used suxamethonium were excluded.

## Results

### Demographic analysis:

We calculated the percentage and frequency of total suspected MH cases in which the frequency of males was 4 while that of females was 3. The rate of male suspected cases was 57.14%, and female was 42.86%, shown in Table 1.

**Table 1: Frequency of Genders**

Gender	Frequency	Percentage
Male	4	57.14
Female	3	42.86
Total	7	100.0

### Frequency of age:

Table 2 shows the age and frequency of patients. We have 7 patients (4 males and 3 females) of different ages. The age of 7 MH suspected patient is 12, 23, 24, 28, 33, 43 and 55. Among them, the percentage of all seven patients was 100 and 14.3 individually for every patient.

### Descriptive Analysis:

Table 3 shows the total number of cases from June 2020 to June 2021 in eight main hospitals at Islamabad and Rawalpindi with a minimum of 1520, maximum of 9360 and mean of 5112.5.

**Table 2: Frequency of age**

Age	Frequency	Percentage
12	1	14.3
23	1	14.3
24	1	14.3
28	1	14.3
33	1	14.3
43	1	14.3
55	1	14.3
Total	7	100

**Table 3: Total Number of cases**

	N	Minimum	Maximum	Mean
Cases	40900	1520	9360	5112.5

The following formula calculated the prevalence of MH:

$$\begin{aligned} \text{Prevalence} &= \text{No. of cases} / \text{total number of cases} \times 100 \\ &= 7/40900 \times 100 \\ &= 0.018\% \end{aligned}$$

### The prevalence rate of MH:

Table 4 shows the prevalence rate of MH in total cases. The total number of surgical patients under GA was 40900, with 7 MH suspected cases. So the prevalence rate was 0.018%.

**Table 4: Prevalence rate of MH**

Total surgical cases under GA	Total MH cases	Prevalence rate
40900	7	0.018%

### Association of MH with other variables:

Table 5 shows an association of MH with gender, in which the male ratio was higher than the female. There were 4 males, and 3 female patients were suspected.

**Table 5: Association of MH with gender**

	Gender		
	Male	Female	Total
MH	4	3	7

**Association of MH with age:**

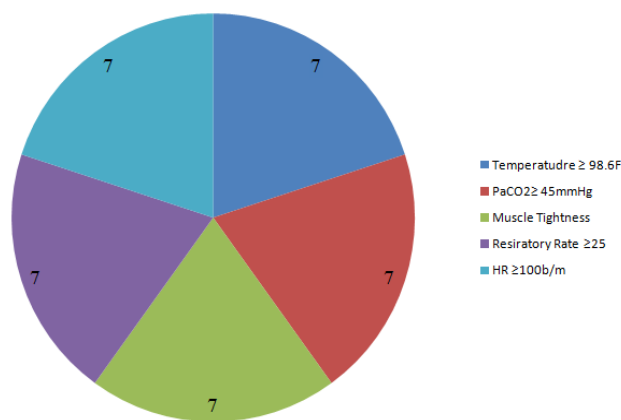
Table 6 MH is associated with age; in which we have seven different ages of patients. The age seven MH suspected patients are 12, 23, 24, 28, 33, 43 and 55.

**Table 6: Association of MH with age**

Age	Age							Total
	12	23	24	28	33	43	55	
MH	1	1	1	1	1	1	1	7

**The severity of MH:**

This chart (Figure 1) shows the severity of MH in total suspected patients out of total surgical cases. The chart shows the temperature, PaCO<sub>2</sub>, muscle tightness, respiratory, and heart rate. The temperature was more significant than 98.6F; the PaCO<sub>2</sub> was greater than 45 mmHg. Muscle tightness during surgery, the respiratory rate was higher than 25, and the heart rate was more than 100b/m.



**Figure 1: Pie chart showing the average percentage of temperature, PaCO<sub>2</sub>, muscle tightness, respiratory rate, and heart rate.**

**Discussion**

This study revealed that the prevalence of MH is scarce in Islamabad, Pakistan. There were 40900 total surgical cases operated under general anesthesia from June 2020 to June 2021 in eight tertiary care hospitals of Islamabad with a minimum of 1520, maximum of 9360, and mean of 5112.5. This research study showed that only seven diagnosed cases of MH were reported out of 40900 surgical cases under general anesthesia. The prevalence rate of MH was 0.018%. According to Brady et al., 12,749,125 patients were discharged from New York state hospitals from 200 to 2006; however, MH was diagnosed in only 73 patients. The percentage of male-diagnosed cases was 57.14%, and that of females was 42.86%, showing that the frequency of MH cases in males versus females is 4:3.<sup>6</sup>

In another study conducted in Japan in 2008, 1,238,171 patients underwent general anesthesia, out of which 344,224 (27.8%) cases were in emergency hospitals and 893,947 (72.2%) in local area hospitals. In this patient population, MH was diagnosed in only 17 patients; the prevalence rate of MH was 0.00138.<sup>15</sup>

Our research study demonstrated that the frequency of males was 4 and females was 3 in total suspected MH cases. Our analysis also revealed that the percentage of male suspected cases was 57.14%, and females were 42.86%. In conformity with the current study's findings, a work done by Masahiko Sumitani stated that male patients were more susceptible to MH than females. According to a recent report by American and Japanese that the prevalence of MH is most common in patients under 30 years of age and less common in patients above 30 years of age.<sup>16</sup>

This research study showed the spectrum of severity, which revealed that the temperature was higher than 98.6F, the PaCO<sub>2</sub> was more than 45 mmHg, there was muscle tightness during surgery, the respiratory rate was higher than 25, and the heart rate was also more than 100b/m. These findings were also investigated in a research study by Brady, J.E in Japan, the first MH models set by the Japanese anesthetist that extensively utilized two variables expanded body temperature increased than 40°C increasing respiratory rate than 25. An increase in

heart rate of 100b/m and other symptoms of MH, muscle tightness, and metabolic acidosis.<sup>6</sup>

## Conclusion

This research study concluded that the prevalence rate of MH at Islamabad and Rawalpindi was 0.018%. The prevalence rate of males is slightly higher than females. The total number of male patients who got MH were four, and female were three out of 40900 surgical cases under general anesthesia in one year. All patients suffering from MH demonstrated severe symptoms of increased temperature higher than 98.6 °F, the PaCo<sub>2</sub> is more than 45 mmHg, muscle tightness during surgery, elevation in a respiratory rate higher than 25, and increased heart rate than 100b/m.

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