

Submitted: October 14th, 2019

Accepted: November 28th 2019

The Incidence and Risk Factors of Carbon Monoxide Poisoning in the Middle East and North Africa: Systematic Review

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ABSTRACT

Background: Carbon monoxide poisoning (COP) represents a significant burden and potential cause of death. However, there are only a few studies about COP in Saudi Arabia despite its noticeable impact on the community.

Objective: This systematic review aimed to estimate the prevalence of COP at the level of Middle Eastern and North African region based on WHO distribution, with a particular interest to extrapolate the case fatality rate (CFR) and complications rates among COP victims.

Methods: By reviewing the databases (Cochrane Library, Pubmed, EMBASE, and CINAHL) in a strategic approach, the relevant studies were retrieved and reviewed independently. Studies were included based on a predefined set of criteria. The quality of each study was evaluated by the Newcastle-Ottawa Scale (NOS). Outcome measures included the incidence (the primary outcome), gender, age, mortality and complications rate, seasonal variations, geographical area, source, and mechanism of exposure.

Results: From 2489 citations, only thirteen studies met the eligibility criteria from five different countries. The date of publication of included studies ranged from 2000 to 2017. The mean sample size was 1483 victims. Most of the victims were females (64.24%). The mean age of the victims was 29.6 years old. The overall incidence of COP was estimated to be equal to 13.37 per 100,000 inhabitants per year. Most of the COP events happened in the winter. Gas heaters were the most frequent source.

Conclusion: COP is still a significant burden though it is potentially preventable. Policies and obligations need reevaluation, and public awareness should be raised.

Keywords: Carbon monoxide poisoning; COP; Case fatality rate; Middle East and North Africa.

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1. INTRODUCTION

The clinical manifestations of carbon monoxide toxicity depend on both the level of carboxylated hemoglobin (HbCO) and the rate and efficiency of a person's breathing, e.g., heavy smokers may already have 9% HbCO. Therefore, HbCO levels of more than 3–4% in non-smokers and more than 10% in smokers are significant.¹ Symptoms range from a mild headache, fatigue, nausea, and vomiting to marked tachypnea, convulsion, hypotension, and eventually death by asphyxiation [1, 2]. Moreover, a percentage of survivors may suffer substantial long-term neurologic and affective complications [3].

Mortalities from carbon monoxide poisoning (COP) mostly result from fires, but around one-third of deaths are attributed to stoves, portable heaters, and automobile exhaust, which is often associated with obstructed or malfunctioning exhaust systems and suicidal attempts [4]. Also, cigarette smoke is considered a significant source of carbon monoxide [4]. Natural gas does not contain CO, but improperly vented gas water heaters, kerosene space heaters, charcoal grills, and hibachis all release carbon monoxide [4]. Other sources of CO exposure include gas-powered concrete saws, inhaling spray paint, and swimming behind a motorboat [4].

Numerous researches have been done to evaluate the epidemiology and risk factors of COP in different areas around the world, but up to our knowledge, no study was conducted as a systematic review except one study from Iran. However, this study included only local studies. This proposed study is going to include all the relevant studies across the Middle East and North African (MENA) countries based on the official divisions of the World Health Organization (WHO). This study aims to assess the incidence and the leading preventable risk factors in the hope that these results could be utilized to improve the overall community health and safety.

2. METHODS

2.1 Search strategy

In this study we reviewed the literature searching for the relevant papers through both subject headings and free-text terms. Databases included PubMed, EMBASE, Cochrane library, and CINAHL. The strategy of search involved three components: (1) prevalence OR incidence OR epidemiology OR emergency department visits, (2) carbon monoxide OR CO; (3) poisoning OR intoxication OR toxicity OR exposure. However, to ensure adequate sensitivity, “carbon monoxide” was used in searching databases that are not sensitive to Boolean operators. Each

database was reviewed independently by at least two authors. Reviewers' task involved identifying the relevant articles and sequentially screening their titles and abstracts for eligibility. Then the retrieved articles were filtered independently by two reviewers against inclusion criteria. A third reviewer solved any disagreements.

2.2 Eligibility criteria

The eligibility criteria involved the following:

2.3 Inclusion criteria:

1. **Type of studies:** any observational study except case reports and case series.
2. **Type of participants:** COP cases in the Middle Eastern Regional Office (EMRO) of WHO.
3. **Type of outcome:** Incidence or prevalence of COP based on the International Classification of Diseases, Ninth Revision (ICD-9) codes 986, E868, E952, or E982 or the International Classification of Diseases, 10 Revision (ICD-10) including codes T58, X47, X67, and Y17.
4. **Outcome measurement:** Studies in which a validated measurement tool was used to screen for and diagnose CO poisoning.
5. **Date of publication:** Up to August 30, 2018

2.4 Exclusion criteria

1. Pediatric or obstetric gynecological studies
2. Natural disaster studies
3. Studies of work-place hazards

2.5 Quality Assessment

For studies that met the inclusion criteria, overall study quality was assessed by the Newcastle-Ottawa scale. Discrepancies in data extraction or assessment of study quality were resolved by consensus discussion between the two primary reviewers with arbitration by a third reviewer as necessary.

2.6 Outcome measures

Outcome measures included the incidence (the primary outcome), gender [n,%] geographical area, source of exposure, age [mean], seasonal variations, cause (accidental, suicide attempts and undetermined), location of incidents (home, workplace, buildings), comorbidities, mortality, the level of carboxylated hemoglobin (HbCO), the use of hyperbaric oxygen therapy (HBOT), and the use of mechanical ventilation.

The overall population size, which is an essential value to calculate the incidence, was estimated by the sum of all populations of the included studies. Data regarding the population size were gained either from information provided in the studies' or mostly by searching google for the population size of each city or area based on its calendar year corresponding to the publication year.

3. Results

3.1 Study selection and study characteristics

Searching through databases revealed 2489 citations. However, the vast majority of them did not meet the eligibility criteria, so they were omitted from the subsequent evaluation. Consequently, 142 articles were surveyed in more detail. After that, only thirteen studies [5-17] were included for critical review and discussion. Three other studies [18-20] provided some useful general information, but they did not provide data regarding our review outcomes. Hand searching of the included articles did not contribute to further articles. The flow chart to select the final thirteen studies is detailed in Figure 1.

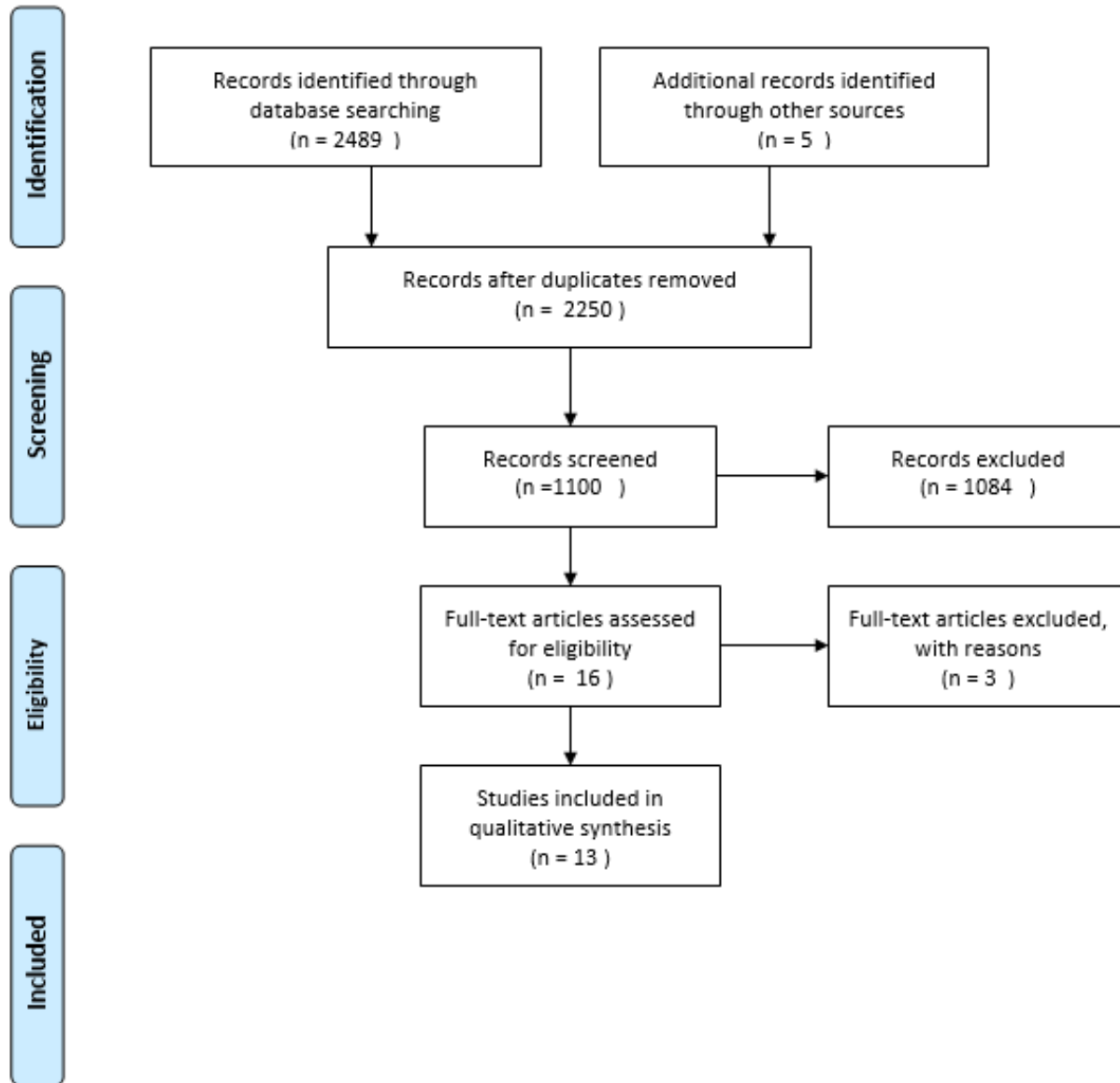


Figure 1: Flow chart of the systematic literature review.

The studies were categorized into three categories based on the assessment of mortality. Seven studies assessed the fatal and non-fatal cases (Group A), five studies assessed only the death cases related to the COP (Group B), and the last two assessed many outcomes, but not the fatality rate (Group C).

Sample sizes ranged from 24 to 12976 subjects across the thirteen studies with the mean of 1483 subjects and a total of 19283 subjects. For each study group, the total numbers were 18105, 1116, and 505 for Group A, B, and C, respectively. Regarding the geographical

distribution, eight studies were conducted in Iran, two in Morocco, and one study in each of the following: Saudi Arabia, Jordan, and Jerusalem.

The date of publication of included studies ranged between 2000 and 2017. The total duration of all included studies was 1055 months. Aghandou and colleagues did the most long-term study with a total duration of 216 months, while the shortest period was 21 months in the study conducted by Yari et al. Table 1 provides data about the country, date of publication, study period, and sample size of included studies, while Table 2 provides data about samples' demographics and the study setting.

First Author	Date of Publication	Study Period (months)	Country	Study Sample
Al-Moamary et al	2000	110	Saudi Arabia	24
Salameh S	2009	144	Jerusalem	292
M. Ait El Cadi	2009	96	Morocco	139
Sheikhazadi A	2010	60	Iran	666
Nazari J	2010	48	Iran	249
Nazari J	2010	60	Iran	3424
Dianat I	2011	24	Iran	1095
Mitra Yari	2012	21	Iran	143
Rachida Aghandous	2012	216	Morocco	12976
Shokrzadeh M	2013	24	Iran	27
Farzaneh E	2015	48	Iran	35
Khadem-Rezaiyan M	2016	84	Iran	443
L.A. Raffee	2017	120	Jordan	213

Table 1: The main characteristics of the included studies

Study	Study setting	Male (n)	Female (n)	Age (mean±SD)	Fatal (%)	Total (n)
Al-Moamary et al	Emergency Department	19	5	35.5±12.5	4.2	24
Salameh S	Emergency Department	144	148	-	0	292
M. Ait El Cadi	Laboratory of forensic toxicology	77	62	-	100	139
Sheikhazadi A	Legal Medical Organization (LMO)	456	210	29.2±15.1	100	666
Nazari J	-	135	114	32.8±20.5	100	249

Nazari J	Ambulance dispatch centres	1361	2063	-	10.1	3424
Dianat I	-	367	728	-	8.22	1095
Mitra Yari	Tertiary Hospital	52	91	-	21.7	143
Rachida Aghandous	Poison centre	4325	8651	25.5±15.6	0.9	12976
Shokrzadeh M	Department of Forensic Medicine	17	10	29.2±15.1	100	27
Farzaneh E	-	16	19	33.7±21.4	100	35
Khadem-Rezaiyan M	Toxicology department	268	175	32.3±18.2	5	443
L.A. Raffee	Tertiary Hospital	50	71	26	0	121
	Poison Centre	50	42	25.5	0	92

Table 2: The primary demographics of samples across the included studies

Study	Selection (max. 4 stars)	Comparability (max. 2 stars)	Outcome (max. 3 stars)	Total Score
Al-Moamary et al	★★★	-	★★★	6/9
Salameh S	★★★	-	★★★	6/9
M. Ait El Cadi	★★★	-	★★★	6/9
Sheikhazadi A	★★★	-	★★★	6/9
Nazari J	★★★	-	★★★	6/9
Nazari J	★★★	-	★★★	6/9
Dianat I	★★★	-	★★★	6/9
Mitra Yari	★★★	-	★★★	6/9
Rachida Aghandous	★★★	-	★★★	6/9
Shokrzadeh M	★★★	-	★★★	6/9
Farzaneh E	★★★	-	★★★	6/9
Khadem-Rezaiyan M	★★★	-	★★★	6/9
L.A. Raffee	★★★	-	★★★	6/9

Table 3: The quality of the included studies based on the Newcastle-Ottawa Scale

Since all studies follow the same study design, which is a single-arm retrospective cohort, the studies have universally moderate quality as assessed by the Newcastle-Ottawa scale. See Table 3.

3.2 The demographic characteristics of the Victims

3.2.1 Gender

The overall distribution of cases based on gender showed that females represented 62.8% (n=12389) of the victims. As mentioned earlier, studies were classified into three groups. In Group A (studies that looked at fatal and non-fatal COP cases), the results seem to be similar to the overall distribution, in which the females were the majority (64.7%, n=11713). However, in the post-mortem studies (Group B), the distribution was almost the opposite, and the females represented 37.2% (n=415) of the cases. In Group C, the results seem to be exceptional, since the distribution between females (51.7%, n=261) and males were almost equal.

3.2.2. Age

The range of victims' age was not mentioned in the included studies, and eight studies merely calculated the mean age of the victims. Overall, the mean age was 29.6 years. At the level of individual groups, the mean age was 31.1, 30.4, 25.7 in groups A,B, and C, respectively. However, only three from group A, four from group B, and one from group C that reported the mean age.

3.2.3 The overall incidence of COP

The overall population size was estimated at 55,734,402 based on the calendar year of each study. The total number of diagnosed COP cases were 19726, among whom 1722 cases were fatal (9.6%). The overall incidence rate of COP was estimated based on the results of group A studies since they investigated all cases of fatal and non-fatal COP. The total duration of these studies was 515 months (ranged between 21 and 216 months), and the aggregated population size based on these studies calendar year was estimated at 47,780,000. The total number of reported cases in group A was 6392, which equals to an incidence rate of 13.37 per 100,000 inhabitants.

3.2.4 The case fatality rate (CFR)

The total number of fatal cases reported in groups A and B was 1722 victims (606 and 1116 separately). CFR of individual studies in group A ranged between 0.89% to 21.68%. Since group B involves only the autopsy studies, CFR was 100%.

3.2.5 Pulmonary complications rate

Five studies had assessed pulmonary complications among COP cases. The total number of cases across these studies was 13656 victims, with 6065 (44.41%) had pulmonary complications. Pulmonary complications rates ranged between 9.79% to 45.86%.

3.2.6 Neurological complications rate

Similar to the pulmonary complications, only five studies had assessed the neurological complications among the victims. The total number of cases was 13656 victims, with 8273 (60.58%) had neurological complications. Neurological complications rates ranged between 17.65% to 78.08%.

3.2.7 Gastrointestinal (GI) complications rate

GI complications have been studied in 4 articles with a combined sample size of 13632 cases. After evaluation, the rate of GI complications was 77.56% (n=10573). However, when the rate was evaluated at the level of individual study, it ranged from 14.48% to 80.19%.

3.2.8 Seasonal pattern of COP

Seven of the included studies established that the incidence of COP was the highest during the winter without mentioning the exact month. Nonetheless, two studies did not pay attention to the seasonal variation. The remaining four studies identified the incidence rate by month. The highest incidence was in December, according to Khadem-Rezaiyan et al. and Sheikhzadi et al., while it is the highest in January and February, according to Nazari et al. and El Cadi et al., respectively.

3.2.9 Sources and mechanisms of COP

The conventional sources of COP, as discussed only in seven studies, were gas heaters, charcoal heaters, gasoline motor, fire smoke, cars, kerosene stoves, brazier (Kanun), and sheeshah (local water pipe smoking device, Hubbell-bubble). Out of the thirteen included studies, only ten studies consider the mechanism of inhalation in their outcome of interest. Collectively, the inhalation of CO by victims was accidental (unintentional) in 97.67% of cases, and it was intentional in 2.33% of cases (either suicidal or homicidal). The highest intentional percentage was reported as 12% by Raffee et al., yet none of which was fatal.

3.2.10 Other outcomes

As mentioned before, this study aimed to investigate other additional variables such as the level of carboxyhemoglobin, the location of the event, and how victims were managed [i.e. oxygen mask, intubation, or hyperbaric oxygen therapy (HBOT)]. However, most of the included studies did not provide data regarding these variables. Regarding the use of HBOT, three studies mentioned that 25.4%, 21%, and 17% of patients were treated with HBOT, according to Rachida Aghandous et al., Salameh et al., and Al-Moamary et al., respectively. Concerning the level of HbCO, Salameh et al. found that 71.2% of victims had a HbCO between 5% and 25%, while the remaining 28.8% had a level of greater than 25%.

4. DISCUSSION

This review assessed thirteen manuscripts from five different countries across the EMRO region of WHO. The aim was to estimate the burden of a well-known cause of chemical toxicity, which is CO poisoning. The selection of this specific geographical area counted on the remarkable similarities in geographical, cultural, economic, and lifestyle characteristics along this far-reaching region that extends over the two largest continents. Although some outcomes were almost the same in all included studies such as the seasonal pattern, others were the opposite, e.g., the gender distribution.

Overall, females constituted two-thirds of all COP cases based on the non-autopsy studies. In contrast, autopsy studies showed that two-thirds of victims were males. That may raise the question of why males have a more unfortunate outcome compared to females. Regarding the

most affected age group, data showed that most victims were in their early adulthood, with an average age of thirty years.

This review showed that GI complications, which include nausea and vomiting, were the most prevalent complications among COP victims. This finding may be a result of either a direct or indirect effect of CO on the Chemoreceptor Trigger Zone (CTZ). On the other hand, this high rate of GI complications may be overestimation and not a real reflection of the actual rate due to the subjective method of reporting.

This review showed that gas heaters were the most common source of COP. It reflects that the awareness of the potential hazard of these devices is still under the optimal expectation. However, it is of utmost importance to utilize every possible method to educate the community about the preventive and safety measures regarding these devices, which may hugely influence the future incidence and mortality of COP. However, the included studies have not inspected the level of education of the victims, which might predict education outcomes less reliable.

These findings have great importance in recognizing the burden of the issue and its contributing factors, as well as observing the outcome of victims based on their characteristics. Gas heaters, charcoal heaters, gasoline motor, and fire smoke might be essential tools of daily living activities among the studied populations, although they were the most dangerous sources of COP. Consequently, these hazards should be replaced or at least to be modified. Given that winter is the typical season of such a problem, it urges the policy-makers and community-health practitioners to find the future directions and the current solutions to minimize the potentially preventable hazard in additional efforts during that time of the year. The study also found that COP in this geographical area is almost entirely a result of accidents versus only a very minority of cases, which were either suicidal or homicidal attempts.

A similar review conducted in Iran by Hosseinejad et al. included local studies [21]. The estimated overall incidence rate was 38.91 per 100.000, which is higher than the overall incidence across the MENA region. This review indicates a consistent finding with that of Iranian review regarding the distribution of victims by gender. The Iranian study found that 59.88% of victims were females, while females represented 62.8% of victims in this review. Among the advantages of the Iranian review is the estimation of the proportionate mortality of COP based on the data given by the local legal organization about mortality registration. However, this review lacks the required data to estimate this outcome.

A Portuguese study conducted along eight years by Sá et al. showed a notable difference in the findings [22]. The estimated incidence rate is found to be 5, 86/100000, which is considerably low compared to what both this review and Iranian review had established. Besides, the Portuguese study did not show a considerable variation between the genders of victims; it was almost 1:1 male to female ratio. However, that study concluded that the number of admissions had increased since the inception of hyperbaric oxygen therapy (HBOT), but this review did not provide sufficient data about both hospitalization and HBOT.

Similar to the Portuguese study, a study from Taiwan conducted over 13 years by Huang et al. indicated an equal distribution between males and females' victims of COP [23]. Moreover, their estimated mean age (36 years) was higher than this review's estimation (29.6 years). That study also measured the neurological sequelae among its outcomes of interest. However, there was a significant disparity. Neurological complications were found only in 9.1% of cases in the Taiwanese study, whereas they were found to be in 60.58% of the cases in this review.

In a very recent study done in the USA by Oda G. et al. describing the epidemiology of COP in the Veterans Health Administration healthcare population, the unintentional cases constituted only 72.9% of all cases, while in this review, they constituted 97.7% of the victims [24]. The remaining of the cases were either intentional (10.9%) or undetermined (16.1%). Moreover, most of the victims were males (88.7%), which is the opposite of this paper's findings. Regarding the age group, the USA study demonstrated that almost half of the cases were in their middle adulthood (45-64 years), while in this review, the majority were in their early adulthood. The study also stratified the cases according to the ethnic group, and found that 70.3% were white, 14.4% were black, and 4.6% were Hispanic/Latino.

Although the MENA region includes over twenty countries, the studies were conducted only in seven of them. Many factors may attribute this minimal number of studies. In general, all of the included studies depended on the data registered in the health informatics systems within the region of study. This may indicate that other countries may not have well-established systems in registration or retrieving the data required for these kinds of studies. AlSadon and his colleagues have conducted a systematic review on Health Informatics Technology (HIT) progress in Arab countries, which are the majority in the region [25]. They found that in addition to having access to financial resources, the majority of Arab countries lagged behind in HIT due to the absence of dedicated financial resources and professional incompetence.

Moreover, even in countries with HIT, hospitals must have full audit functions to guarantee the integrity, security, and accuracy of data detained in the records. Bakheet Aldosari conducted a study to evaluate the primary audit capabilities/functions and establish the level of compliance of the electronic health record system installed at one hospital in Saudi Arabia [26]. He found that 12 out of the 17 functions (71%) fulfilled compliance, and five functions received a score of zero (function not in evidence or not user-accessible).

Due to the paucity of research on this topic, this study could represent a starting point for further studies to be done locally and across the MENA region to evaluate the magnitude of carbon monoxide poisoning and its consequences. Also, the results of this study reveal the necessity of developing more effective methods to raise public awareness about COP. Furthermore, the results can encourage developing effective prevention strategies aimed at limiting the dangerous effects of the primary sources of COP in the region.

4.1 Limitations

Three points summarize the main limitations of this study. First, most of the included studies lack essential data in respect of COP. For Example, the level of carboxylated hemoglobin (HbCO), which helps to classify the cases as mild, moderate, or severe, has not been emphasized except in one out of the thirteen included studies. As a result, the association between fatality and severity could not be assessed. Second, English is the only language used in searching for relevant studies. However, the official languages of most MENA countries are Arabic, Persian, and French. As a result, there is a possibility of missing some relevant studies. Nonetheless, one of the included studies was published in the Persian language, and Google translator was utilized to translate it into English.

5. CONCLUSION

In brief, COP affects mostly young people with female predominance, and about one-third of victims had not survived. The most frequent complications associated with COP are gastrointestinal manifestations. Most of the time, the sources of COP are devices used in homes to keep them warm. The incidence is variable all over the year, with the peak is reached in the

winter months. Nevertheless, most MENA countries are still lacking studies about COP prevalence.

6. ACKNOWLEDGMENT

We express our thanks and appreciation to Mr. Najeeb Vattamnthodi, the librarian of King Abdulaziz Medical City, Riyadh, Saudi Arabia, and Mr. Mohammed AlSawadi, the librarian of College of Medicine, King Saud bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia. They both help us in databases search through applying their skills of computer technology and contacting the journals for retrieving the full texts of included studies.

7. CONFLICTS OF INTEREST

None declared

8. FUNDING

Not funded

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