Poisonings at Nepal Medical College Teaching Hospital

B Shrestha,[1] PM Singh,[2] U Bharati[3] and S Dhungel[1]

[1]Department of Medicine, [2]Department of Psychiatry, [3]Department of Casualty and General Practice, Nepal Medical College Teaching Hospital, Kathmandu, Nepal

Corresponding author: Dr. Balaram Shrestha, MD, PhD, Department of Medicine, Nepal Medical College Teaching Hospital, Attarkhel, Jorpati VDC, Kathmandu, Nepal

ABSTRACT

Poisoning is an increasingly common social problem in Nepal. Studies on poisoning in semi urban areas of Nepal are minimal. Here we, present a prospective study of poisoning in semi urban area of capital, Kathmandu lasting for six years duration. Altogether there were 354 cases of various poisoning, admitted in Nepal Medical College Teaching Hospital from Baisakh 2062 (April 16, 2005) to Chaitra 2067 (April 15, 2011). Male: Female ratio was 135:219 (1:1.6) and Age± SD was age 29.3± 13.8 years. Age group (20-29 years) comprised of 138 patients (38.9 % followed by < 20 years age group (92, 25.9%). Brahman/ chhetri (150, 42.4%) and Mongolian (146, 41.2%) ethnic groups were the main sufferers of poisoning, followed by newars (41, 11.6%) patients. Deliberate self harm was the cause for poisoning in maximum number of patients (156, 44.1%), followed by depression (64, 18.1%) and accidental poisoning (42, 11.9%). Organophosphorus (152, 42.9%), medicines (71, 20.1%), and rodenticide poisoning (38, 10.7%) were common poisons. Metacid (Methyl parathion) (46, 15.5%) was the most popular brand of poisoning agent used in Nepal for suicidal purpose. The over all mortality rate of poisoning in general was 7.1% with organophosphorus poisoning topping the list (19, 12.5%). We also present mad honey poisonings in a small group of 9 (3.2%) patients with M:F 8:1, age 26.5±8.8 years. Due precaution should be undertaken during their management as some of them may go into cardiopulmonary arrest and should not be considered benign when more than 5 tablespoonful wild honey is consumed.

Keywords: Poisoning, organophosphorus poisoning, mad honey poisoning, grayanotoxin, deliberate self harm.

INTRODUCTION

Every year, almost one million people die from suicide with a "global" mortality rate of 16 per 100,000. In the last 45 years suicide rates have increased by 60% worldwide. Suicide is among the three leading causes of death among those aged 15-44 years in some countries.[1]

Studies on poisoning in semi urban areas of Nepal are rare.[2-5] Here, we present a prospective study of poisoning in semi urban area, Jorpati village development committee, (JVDC) of the capital, Kathmandu lasting for six years duration. This may be the largest prospective study performed in poisoning in Nepal. Out of them, we also observed a small group of poisoning due to mad honey poisoning, which is considered rare and limited to few case reports in Nepal.[6,7]

PATIENTS AND METHODS

This was a prospective study of poisoning in semi urban area (Jorpati VDC) of the capital of Nepal. Altogether there were altogether 354 patients suffering from various poisonings during the six years observation period from Baisakh 2062 (April 16, 2005) to Chaitra 2067 (April 15, 2011) were admitted in Nepal Medical College Teaching Hospital (NMCTH) during the period, were enrolled as study subjects. Charts of the patients were used for socio-demographic assessment and clinical parameters evaluation. Ethnic group-wise distribution, age-group wise distribution, poisoning agent consumed, reason for poisoning and their out comes were evaluated. As a subgroup analysis of a small group of mad honey poisoning was also performed with the evaluation of age, gender, amount of mad honey consumed, clinical features of mad honey poisoning, treatment given and outcome of treatments.

RESULTS

There were altogether 354 patients suffering from various poisonings during the six years observation period in NMCTH. Male: Female ratio was 135:219 (1:1.6). Mean age ± SD was 29.3 ± 13.8 years.

Age and gender wise distribution of poisoning is shown in Fig. 1. Age group (20-29 years) comprised of largest number of patients (138, 38.9 %) followed by < 20 years age group (92, 25.9%). Poisonings were more common in females in almost all age groups except the age group of 50-59 years (Fig. 1).

Ethnic group wise distribution of various poisonings in NMCTH is shown in Fig. 2. *Brahman/ chhetri* (150, 42.4%) and Mongolian ethnic group (146, 41.2%) were the main sufferers of poisoning followed by *newars* (41, 11.6%).

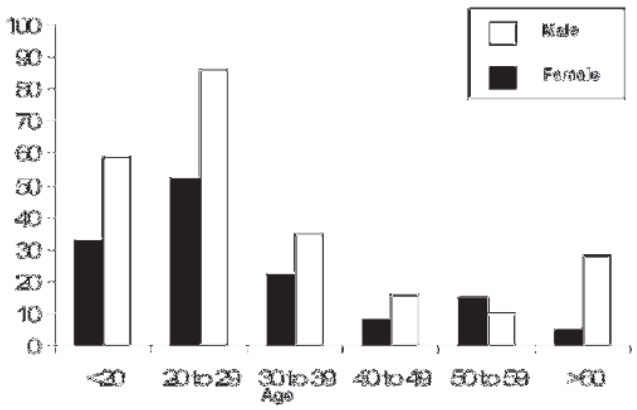

Fig. 1. Bar diagram showing age wise distribution of various poisonings

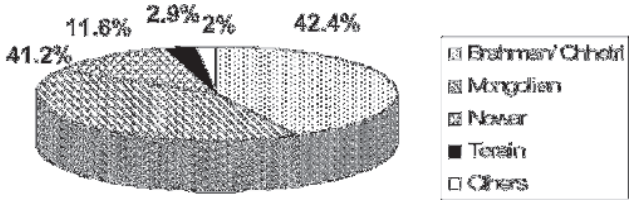

Fig. 2. Ethnic group wise distribution of poisoning in NMCTH

Poisoning agents used in NMCTH is shown in Fig.3. Organophosphorus poisoning (150, 42.4%), drugs (71, 20.1%) and rodenticides (40, 11.3%) were common poisons. Metacid (Methyl parathion) is the most popular brand for poisoning agent used in our study (61, 17.2%). Other common agents are cypermethrine (6, 4.5%), zinc phosphide (13, 3.7%) and paracetamol (21, 5.9%).

Reasons for poisoning are shown in Table-1. Deliberate self harm (156, 44.1%) was the commonest cause for poisoning, followed by depression (64, 18.1%) and accidental poisoning (42, 11.9%). Deliberate self harm was 3 times more common in females (Male: Female = 39: 117 or 3:1).

Outcome and Poison wise mortality rates at NMCTH are shown in Table-2.

Organophosphorus is the most common poisoning agent used in NMCTH with the maximum mortality (19, 12.7%).

Table-3 shows summary of a small group of 9 patients suffering from wild honey poisoning in Nepal Medical College Teaching Hospital. Nine patients were admitted in Nepal Medical College Teaching Hospital during Baisakh 2062 (April 16, 2005) to Chaitra 2067 (April 15, 2011). Male female ratio was 8:1 and mean age ± SD was age 26.5 ± 8.8 years. Some even attempted to consume 10 tablespoonful or more of wild honey and almost died of severe intoxication. Table-3 shows age, gender, amount of honey consumed, symptoms developed and medications given to resuscitate them.

DISCUSSIONS

Poisoning is an increasingly common social problem in developing countries like Nepal.[8] Studies on poisoning in semi urban areas of Nepal are rare.[2-5] This prospective study of poisoning elaborated various aspects of poisoning around Jorpati VDC situated in semi urban area of the capital, Kathmandu lasting for six years duration. This may be the largest prospective study of poisoning in Nepal.

Poisoning was noted more in females in all age groups as shown in Fig.1 with overall male: female ratio being 1:1.6. Similar higher prevalence of poisoning in females were previously reported.[2-5] The reason for this finding may be that females were more emotionally unstable. They were usually economically dependent on males. They were more sufferers of domestic violence as well. Multi-marriage is quite common in Mongolian ethnic group.[9] Indian report however, showed higher rates of poisoning of males (93:55) in comparison to females. It

Table-1: Reasons for poisoning in NMCTH

Causes for poisoning	n. (%)
Deliberate self harm	156 (44.1)
Depression	64 (18.1)
Accidental	42 (11.9)
Substance dependence syndrome	30 (8.5)
Adjustment disorder	28 (7.9)
Acute stress reaction	4 (1.1)
Psychosis	12 (3.4)
Epilepsy	9 (2.5)
Homicide	9 (2.5)
Total	354 (100)

Table-2: Poison wise mortality rates at NMCTH

Poisoning agents consumed	n.	Death	Mortality (%)
Organophosphorus	150	19	12.7
Rodenticides	40	1	2.5
Medicines	71	1	1.4
Alcohol	18	2	11.1
Chemicals	27	2	7.4
Mushroom	13	0	0
Wild honey	9	0	0
Substance abuse	5	0	0
Unknown	21	0	0
Total	354	25	7.1

Table-3: Wild honey poisoning in NMCTH

Case	Amount of wild honey consumed (1 tablespoonful, tbsf = 15 ml)	Interval between consumption of honey and appearance of symptoms	Symptoms and signs of honey poisoning as observed before/ during hospitalization	Treatment given for wild honey poisoning during hospitalization
1. 25/ M	10 tbsf (Had half dinner; fried rice, egg after consuming honey)	10 minutes to 90 minutes	Felt nausea, burning sensation in throat, wretching, vomiting (4), shortness of breath, gasping breath, apnea, palpitation, blackout, loss of consciousness, rushed to ER in a mbulance, gasping breath, with apnoeic episodes, loss of consciousness,dilatation of pupils, not reacting to light, PR= absent ??, BP 60/?? mm Hg, SpO_2 2-64%, Chest/CVS/P/A normal. ECG: ST elevation in lead II, III, aVF, suggestive of inferior wall MIIn ICU, restless, pupils dilated, reacting sluggishly to the light, BP 88/44, 106/78, 106/59 mm HgFollow up echo suggestive of inferior wall myocardial infarction.	Inj. NS 500 ml IV, Inj. RL 1000ml IV, Inj Adrenaline 0.3 ml S/C, IV atropine, IV Dopamine infusion @ 8 µg/kg/min, Inj Hydrocortisone 200 mg IV + 100mg IV TDS (3days), Inj Pheniramine maleate 45.5 mg IV, Inj. Ranitidine 50 mg IV, Inj Metochlopramide 10mg IV, O_2 inhalation @ 3L/min. Regained consciousness after s/c adrenaline, IVdopamine infusion (2 pm). Discharged after 2 days of management for extreme bradycardia, hypotension, ? inferior wall myocardial infarction.
2. 24/ M	8 tbsf (Had full dinner along with honey).	10 minutes to 90 minutes	Burning sensation in throat, flushing of face and body, Dizziness, headache, nausea, vomiting (3), blackouts, sweating, shivering, dryness of mouth and throat, loss of consciousness, vision, diplopia, pupils dilated and sluggishly reactive to light, unconscious, peripheral pulses not palpable, carotid pulse feeble and 35/min, BP not recordable. In ICU: PR = 64/min, BP 100/60 mm Hg, Sp O_2 92%, pupils: dilated and reacting sluggishly to light, dizziness, diplopia, chest/ CVS/ P/A: normal.	Inj. NS 500 ml IV, Inj Adrenaline 0.3 ml s/c, Dopamine infusion @ 8 µg/kg/min, Inj Hydrocortisone 200 mg IV, Pheniramine maleate 45.5 mg IV, Inj Ranitidine 50 mg IV, Inj Metochlopramide 10mg IV, O_2 Inhalation @ 3L/min. He was admitted for observation and discharged after 2 days.
3. 24/ M	5 tbsf	1 hour	Vomiting (3 episodes), diplopia, dizziness, blurring of vision, blackouts, loss of consciousness, BP 110/80 mm Hg, PR 82/min, temperature 98° f, Pupils: dilated pupils and reacting sluggishly to light, chest/ CVS/ P/A: normal.	Inj. NS 500 ml, RL 1000 ml IV, Inj Ranitidine 50mg IV, Pheniramine maleate 45.5 mg IV, Inj Metochlopramide 10mg IV, O_2 inhalation @3L/min. He was admitted for observation and was discharged after 24 hours.
4. 22/ M	3 tbsf	1 hour	dizziness, blurring of vision, Dilated pupils which is sluggishly reacting to light.Chest/ CVS/ P/A: normal	Inj. NS 500 ml, RL 1000 ml IV infusion. He was admitted for observation and discharged after 1 day.
5. 22/ M	3 tbsf	1 hour	dizziness, blurring of vision, vomiting bradycardia (78/min), hypotension (100/70 mm Hg) temperature 97° f, Chest/ CVS/ P/A normal. Drowsy for 1 hour.	Inj. NS 1000 ml IV, RL 1000 ml IV , Pheniramine maleate 45.5 mg IV, Ranitidine 50 mg IV, Inj Metochlopramide 10mg IV, Inj Hydrocortisone 100 mg IV, O_2 inhalation @ 3/ min. He was admitted for observation and discharged after 24 hours.
6. 23/ M	2 - 3 tbsf	90 minutes	Vomiting (2 episodes), dizziness, diplopia, blurring of vision, bradycardia (48/min), hypotension (80/40 mm Hg), Pupils: dilated and reacting sluggishly to light, Chest/ CVS/ P/A: normal.	Inj. NS 500 ml IV, Inj. RL 1000 ml IV, Pheniramine maleate 45.5 mg IV, Ranitidine 50 mg IV, Inj Metochlopramide 10mg IV, Inj Hydrocortisone 100 mg IV, O_2 inhalation. He was admitted for observation and discharged after 24 hours.
7. 24/ M	2 - 3 tbsf	90 minutes	Vomiting, dizziness, diplopia, blurring of vision, bradycardia (48/min), hypotension (80/40 mm Hg), Temperature 97° f, Pupils: dilated and reacting sluggishly to the light, Chest/ CVS/ P/A: normal.	Inj. NS 500 ml IV, Inj. RL 1000 ml IV, Pheniramine maleate 45.5 mg IV, Ranitidine 50 mg IV, Inj Metochlopramide 10mg IV, Inj Hydrocortisone 100 mg IV, O_2 inhalation @ 3L/min. He was admitted for observation and discharged after 24 hours.
8. 33/ M	20 ml	1hr	epigastric pain, dizziness, blurring of vision, weakness, chest pain, vomiting 5 times, fall on the ground, PR = 36/min, BP=90/60 mm Hg, repeat PR = 32/min, pr 112/min, BP = 150/110mm Hg after inj atropine, RR= 24/min, Chest/ CVS/ P/A: normal.	Inj atropine 0.6mg iv stat and SOS, DNS 1000 ml, NS 500 ml 12 hourly. He was discharged after observation for 24 hours.
9. 48/F	20ml	½ hr	Vomiting, loose stool, headache, vertigo, epigastric pain, semiconscious, PR= 80/min, RR= 20/min BP = 88/66 mm hg, PR= 84/min, BP= 60/40mmg Hg, sp O_2 90 without O_2.	Inj. NS 1500 ml IV, Inj Hydrocortisone 200mg IV, Pheniramine maleate 45.5 mg IV. She was discharged after 24 hours of observation.

may be related with higher stressful lives in India than in Nepal. Presence of dowry (*dahej*) system draining fathers or brothers of a bride financially. This social problem may have resulted in higher abortion of daughters intrauterine and tilting the natural balance of males and females in their society.

Brahman/chhetri (150, 42.4%) and Mongolian ethnic group (146, 41.2%) were the main sufferers of poisoning, followed by newars (41, 11.6%) as shown in fig 2. Poverty and illiteracy/ ignorance could be the cause. Higher prevalence of rampant poverty, illiteracy and family problems (especially marital disharmony, early marriage, extramarital affairs, multiple marriages, were quite common among immigrant Mongolian people residing around NMCTH. Despite being quite close to mongolian communities, poisoning in newars seems a bit low probably because of better family support and economic prosperity among newars.

Organophosphorus poisoning and rodenticides were common poisoning agent used in Nepal (Fig.3). This finding is compatible with other papers from Nepal.[2-5] The cause for it could be due to easy availability of organophosphorus and rodenticides in the general shops or agricultural depots. Among all poisoning agents, Metacid (Methyl parathion) was the most popular brand of organophosphorus followed by Nuvan and cypermethrine. Zinc phosphide (rodenticide) was also commonly used because of its easier access and availability. Medicinal poisoning had reached to second position (Fig.3). This finding may support the changing health scenario with increased hospitals, medical shops and easier access of various medicines to general people.

Prevention of poisoning by restrictions in access to dangerous means for suicide were likely to play an important role in reducing suicide rates in Denmark, especially for women.[10] To prevent easy access, substances like organophosphorus and rodenticides should not be sold to younger females (up to 40 years). Rules mimicking sales of liquor banning to under age groups may be useful for controlling poisoning in younger females. Uncontrolled and unrestricted sales of almost all medicines as over the counter medicines should be closely supervised and restricted to the real needy patients with prescriptions so as to control poisoning with medicines. Limiting amount of psychotropic medicines may be beneficial to avoid poisoning or overdose of psychotropic medicines to psychiatric patients.

Causes for poisoning in NMCTH is shown in Table-2. Almost all cases of poisoning were related to some psychiatric illnesses or susceptibility towards them. Deliberate self harm (156, 44.1%) was the commonest cause of poisoning in NMCTH. Similar report has been reported from western Nepal. Poisoning (89.6%) was the most preferred method of deliberate self-harm. [11] Deliberate self harm was 3 times more common in females (Male: Female = 39: 117 or 3:1)

Depression (64, 44.1%) and adjustment disorder (28, 7.9%) were other causes for poisoning. Depression and psychosocial stress were previously reported as important causes of suicide.[3] Psychiatric consultation and support is hence very crucial in the management of poisoning in Nepal. Homicidal poisonings (9, 2.5%) were mainly confined to the efforts made by robbers to rob people by giving some juice mixed with unknown substance to drink or some sweets mixed with unknown substance to eat. Accidental poisoning was found in a significant number (42, 11.9%).

Mortality rate due to poisoning has been reported to be only 1% to 2% in developed countries but in developing countries it is 15% to 30%. [9] Mortality rate of acute poisoning in NMCTH was 7.1%. It is a bit higher in comparison to previous report of 5% and 5.6%.[2,4] The reason may be due to poverty and ignorance of the local inhabitants. Mongolian ethnic group (e.g. Tamangs) immigrated from rural area (e.g. Sindhupalchowk) to the nearby locality of NMCTH for working in local carpet factories. They may have rampant poverty and social ignorance, resulting in delay in treatment of poisoning and many times, leaving hospital without medical advices are quite common. Other hospitals are located in more affluent societies. Organophosphorus had the maximum mortality (Table 2). Mortality in organophosphorus poisoning is still higher than other reports. [2, 4] This finding may probably due to rampant poverty, social ignorance, disorganized traffic jams and lack of efficient ambulance facilities resulting in the delay to rush for emergency management of poisoning and many times leaving hospital without medical advice even after hospitalization.

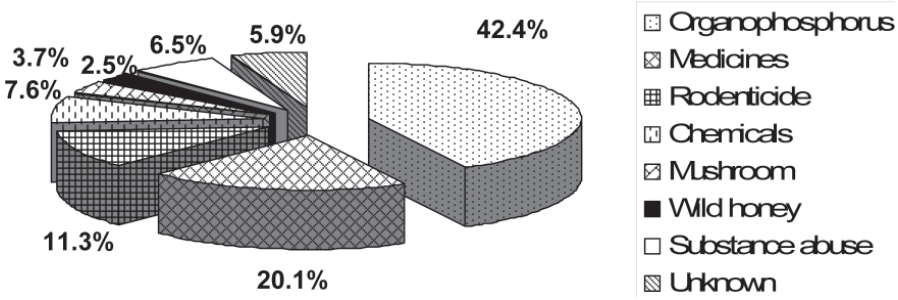

Fig. 3. Poisoning agents used in NMCTH

Higher mortality rate observed in patients intoxicated with alcohol (Table-2) may be due to other concomitant disease with poor prognosis such as cirrhosis of liver. This finding is not strange in the back ground of excessive alcohol consumption in the Mongolian people residing around the NMCTH.

Honey has been used since ancient times for several of its nutritive and therapeutic properties. It is an effective antitussive,[12] improves glycemic control,[13] has cardio protective and vasoactive properties.[14] It has hepatoprotective, renoprotective effects as well[15] as gastroprotective effect.[16] It has antioxidant effect with better radical scavenging activity.[17,18] It has antibacterial effects as well[19,20] Honey is found to be useful in wound healing.[21, 22] Honey enhances immune function and has anti tumor activity.[23,24]

Wild honey intoxication, also called as rhododendron poisoning or mad honey poisoning, is caused by the consumption of honey produced from the nectar of rhododendrons.[25] It is usually seen in the Black Sea region of Turkey.[26-29] Mad honey poisoning causes especially various cardiac effects such as hypotension, bradycardia, complete heart block, nodal rhythm.[30-34] They can be managed with short observation in emergency department or intensive care unit.[32] Sometime it can also cause acute myocardial infarction.[33]

Honey intoxication in the land of rhododendron should be common, however, their reporting in hospitals of Nepal is not common and are limited to few case reports only.[6,7] Our report of 9 cases of mad honey poisoning (Table-3) may be the largest number of mad honey poisoning in Nepal. Male female ratio was 8:1 and mean age ± SD was age 26.5 ± 8.8 years. Majority of patients were few adventure seeking young medical students who despite warning of the possibility of getting drowsy just like alcohol, consumed wild honey in unusually large amount at the peak time of hunger just before having their dinner after whole day of heavy physical exertion during the festival of colors (Holi). Some even dared to consume 10-15 tablespoonful of wild honey and almost died of severe intoxication. After 10 to 90 minutes, patients developed various symptoms ranging from mild gastric irritation to extreme bradycardia, hypotension and loss of consciousness. They had to be resuscitated with cardiopulmonary resuscitation and some emergency medicines such as atropine, adrenaline, dopamine infusion, intravenous fluids. Some of the extremely symptomatic patients were initially considered to have suffered from anaphylactic reaction to wild honey by the emergency on duty doctor and treated accordingly. Later on, they were treated with atropine along with parenteral fluids and other symptomatic treatments. Luckily all patients could be saved as they reside near the hospital and were immediately brought to hospital emergency department. Some patients with minimal poisoning with 2-3 tablespoonful mad honey could be simply resuscitated with just parenteral fluid therapy alone.

Wild honey poisoning may be dangerous if is consumed 5 tablespoonful or more. They may have extreme bradycardia, hypotension, labored breathing, apnoeic spells, and loss of consciousness when the amount reaches 10 tablespoonful especially when consumed during fasting period. However, consumption less than 3 tablespoonful may not be that dangerous and may be managed simply by parenteral hydration with or without the need of atropine. Inj. Atropine, parenteral hydration with normal saline were useful to treat them however, some patients with persistent hypotension and bradycardia were treated with inj. Adrenaline and dopamine infusion. 24 to 48 hour observation were adequate and were discharged from hospital.

Mad honey poisoning is relatively rare in the Himalayan country Nepal which grow its national flower rhododendron (Lali gurans) along its mountainous region. However, mad honey poisoning may be dangerous due to its severe cardiovascular symptoms like extreme bradycardia, hypotension and fainting. Despite warning of the possibility of getting drowsy just like alcohol, few adventure seeking young medical students attempted to consume wild honey in unusually large amount at the peak time of hunger on fasting state before eating meal. Some even attempted to consume 10 tablespoonful or more of wild honey and almost died of severe intoxication. Over enthusiasm and adventure seeking tendency may end up with death in apparently milder looking honey poisoning.

Poisoning is an increasingly common social problem in Nepal. Use of organophosphorus or rodenticide are common poisoning agent used for suicidal purpose. One of the cause for it may be due to easy accessibility of these agent in local market. Limiting the access to these common poisoning agent in vulnerable age group may be useful step to prevent poisoning. Development of specific manpower like spraying insecticides with all due precautions and not selling insecticides, rodenticides to vulnerable age group (15-40 years) is recommended. There is an urgent need for strict implementation of the pesticide control act, so that it could strengthen the legislature on availability of drugs and poisons in the market. Introducing separate toxicological units in the hospitals and upgrading the peripheral health centres to manage cases of poisoning in emergency could possibly help us to bring down the mortality and morbidity rates.

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REFERENCES

1. WHO: Mental Health: Suicide prevention. http://www.who.int/mental_health/prevention/suicide/suicideprevent/en/index.html (Accessed on 29th November 2011.)
2. Paudyal BP. Poisoning: pattern and profile of admitted cases in a hospital in central Nepal. *J Nepal Med Assoc* 2005; 44: 92-6.
3. Chakrabarti K, Devkota KC. Retrospective study of suicide cases admitted in Nepal Medical College Teaching Hospital. *Nepal Med Coll J* 2004; 6: 116-8.
4. Marahatta SB, Singh J, Shrestha R, Koju R. Poisoning cases attending emergency department in Dhulikhel Hospital-Kathmandu University Teaching Hospital. *Kathmandu Univ Med J* 2009; 7: 152-6.
5. Khadka SB, Khadka SB. A study of poisoning cases in emergency Kathmandu Medical College Teaching Hospital. *Kathmandu Univ Med J* 2005; 3: 388-91.
6. Shrestha P, Vaidya R, Sherpa K. Mad honey poisoning: a rare case report of seven cases. *Nepal Med Coll J* 2009; 11: 212-3.
7. Dubey L, Maskey A, Regmi S. Bradycardia and severe hypotension caused by wild honey poisoning. *Hellenic J Cardiol* 2009; 50:426-8.
8. Sayami A, Shrestha B. Toxicology. In Sayami A, Shrestha B. Critical care Manual of ICU/CCU T U Teaching Hospital (1st ed.). Kathmandu: JICA Medical Education Project 1995; 130-43.
9. Kiran N, ShobhaRani RH, JaiPrakash V *et al*. Pattern of poisoning reported at south Indian tertiary care hospital. *Indian J of forensic medicine and toxicol* 2008; 2: 7-12.
10. Nordentoft M. Prevention of suicide and attempted suicide in Denmark. Epidemiological studies of suicide and intervention studies in selected risk groups. 2007, *Dan Med Bull* 54:306-69.
11. Subba SH, Binu VS, et al. Pattern and trend of deliberate self-harm in western Nepal. *J Forensic Sci* 2009 May; 54(3):704-7.
12. Paul IM, Beiler J, McMonagle A, Shaffer ML, Duda L, Berlin CM Jr. Effect of honey, dextromethorphan, and no treatment on nocturnal cough and sleep quality for coughing children and their parents. *Arch Pediatr Adolesc Med* 2007; 161: 1140-6.
13. Erejuwa OO, Sulaiman SA, Wahab MS, Sirajudeen KN, Salleh MS, Gurtu S. Glibenclamide or metformin combined with honey improves glycemic control in streptozotocin-induced diabetic rates. *Int'l J Biol Sci* 2011; 7: 244-52.
14. Rakha MK, Nabil ZI, Hussein AA. Cardioactive and vasoactive effects of natural wild honey against cardiac malperformance induced by hyperadrenergic activity. *J Med Food* 2008; 11: 91-8.).
15. EI Denshary ES, Al-Gahazali MA, Mannaa FA, Salem HA, Hassan NS, Abdel-Wahhab MA. Dietary honey and ginseng protect against carbon tetrachloride-induced hepatonephrotoxicity in rats. *Exp Toxicol Pathol* 2011 Feb 15 (Epub ahead of print).
16. Bukhari MH, Khalil J, Qamar S *et al*. Comparative gastroprotective effects of natural honey, Nigella sativa and cimetidine against acetylsalicylic acid induced gastric ulcer in albino rats. *J Coll Physicians Surg Pakistan* 2011 ; 21: 151-6.
17. Kishore RK, Halim AS, Syazana MS, Sirajudeen KN. Tualang honey has higher phenolic content and greater radical scavenging activity compared with other honey sources. *Nutr Res* 2011;31: 322-5. (Epub 2011 Apr 13).
18. Erejuwa OO, Sulaiman SA, Wahab MS, Salam SK, Salleh MS, Gurtu S. Comparison of antioxidant effects of honey, glibenclamide, metformin and their combinations in the kidneys of streptozotocin-induced diabetic rats. *Int J Mol Sci* 2011; 12: 829-43.
19. Deshpande SD, Kulkarmi KS. In vitro effect of some Indian honeys on Staphylococcus auresu from wounds. *Indian J Exp Biol* 1010; 48: 931-5.
20. Cooper RA, Molan PC, Harding KG. The sensitivity to honey of Gram-positive cocci of clinical significance isolated from wounds. *J Appl Microbiol* 2002; 93: 857-63.
21. Lee DS, Sinno S, Khachemoune A. Honey and wound healing; an overview. *Amer J Clin Dermatol* 2011; 181-90.
22. Al-Waili N, Salom K, Al-Ghamdi AA. Honey for wound healing, ulcers, and burns; data supporting its use in clinical practice. *Scientific World J* 2011; 11: 766-87.
23. Fukuda M, Kobayashi K, Hirono Y *et al*. Jungle Honey enhances immune function and antitumor activity. *Evid Based Complement Alternat Med* 2011; 2011: 908743.
24. Samarghandian S, Afshari JT, Davoodi S. Honey induces apoptosis in renal cell carcinoma. *Pharmacogn Mag* 2011; 7: 46-52.
25. US Food and Drug Administration Center for food safety and applied nutrition. Food borne pathogenic microorganisms and natural toxins handbook. (http://www.cfsan.fda.gov/~mow/chap44.html).
26. Bostan M, Bostan H, Kaya AO *et al*. Clinical events in mad honey poisoning: a single centre experience. *Bull Environ Contam Toxicol* 2010; 84: 19-22 (Epub 2005 Nov 25).
27. Koca I, Coca AF. Poisoning by mad honey: a brief review. *Food Chem Toxicol* 2007; 45. (Epub 2007 Apr 21)
28. Gunduz A, Turedi S, Russell RM, Ayaz FA. Clinical review of grayanotoxin/mad honey poisoning past and present. *Clin Toxicol (Phila)* 2008; 46: 437-42.
29. Okuyan E, Uslu A, Ozan Levent M. Cardiac effects of "mad honey": a case series. *Clin Toxicol (Phila)* 2010; 48: 528-32.
30. Cagli KE, Tufekcioglu O, Sen N *et al*. Atrioventricular block induced by mad-honey intoxication: confirmation of 31 diagnosis by pollen analysis. *Tex Heart Inst J* 2009; 36: 342-4.
31. Weiss TW, Smetana P, Nurnberg M, Huber K. They honey man – second degree heart block after honey intoxication. *Intl J Cardiol* 2010; 142: e6-7. (Epub 2008 Dec 18).
32. Gunduz A, Durmus I, Turedi S, Nuhoglu I, Ozturk S. Mad honey poisoning-related asystole. *Emerg Med J* 2007; 24: 592-3.
33. Gunduz A, Merice ES, Baydin A, Topbas M, Uzun H, Turendi S, Kalkan A. Does mad honey poisoning require hospital admission? *Amer J Emerg Med* 2009; 27: 424-7.
34. Ajubcu S, Arslan U, Karakurt K, Cengel A. An unusual presentation of mad honey poisoning: acute myocardial infarction. *Int'l J Cardiol* 2008; 129: e56-8. (Epub 2007 Sep 24)