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Research Article

Traditional Unani Medicine in Flu-like Epidemics and COVID-19 during Pregnancy: A Literary Research

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ABSTRACT

Background: The pandemic COVID-19 caused by a novel coronavirus SARS-COV-2 has spread like a forest fire. This disease may have serious consequences for pregnant women. Presently, no specific drugs or vaccines exist to battle this disease and researches are underway. Unani medicine has a unique role in prevention and management during epidemics. Here, we reviewed the overview of COVID-19 infection and pregnancy, concept and practices in Unani medicine for flu-like epidemics in general and pregnancy, and safety of Unani drugs for the prevention and treatment of mild symptomatic cases of COVID-19 during pregnancy.

Methodology: Unani classical texts and pharmacopoeia were meticulously explored for concepts and practices for flu-like epidemic diseases. Further, we browsed scientific databases such as PubMed, Scopus and others for an overview, epidemics and Unani medicine, effectiveness and safety of Unani drugs in COVID-19 and pregnancy.

Results: Unani medicine includes prevention and management of flu-like epidemic include quarantine and isolation, aromatic herbal drugs fumigation and spraying for environmental disinfection, ilaj bid tadbir for health promotion and use of health-protecting drugs and symptom-specific drugs in general and related to pregnancy. Lahsun, asalussus, behidana, banafsha, zanjabeel, unnab, etc are in use since antiquity for the prevention and treatment of asymptomatic and mildly symptomatic pregnant women during infectious and epidemic diseases.

Conclusion: Currently, the aforementioned plants are proven for antiviral, antioxidant, immunomodulatory and anti-inflammatory activities, probably useful in the COVID-19 pandemic. Additionally, scientific studies have provided new insight into the mechanism underlying the therapeutic effect of Unani medicines that are safe in pregnancy.

Keywords Antiviral herbs, COVID-19 and pregnancy, Climate change/weather, Flu-like epidemic, Pandemic, *Waba*

INTRODUCTION

There are seven coronaviruses presently infecting humans. SARS-CoV-2 is the third most common coronavirus after Severe Acute Respiratory Syndrome (SARS) and the Middle East Respiratory Syndrome (MERS) to cause major epidemics (Zhao *et al.*, 2020) known as COVID-19. WHO on January 30, 2020, declared the novel coronavirus COVID-19 outbreak as a public health emergency of International Concern, which was first detected in Wuhan, China on December 31, 2019. This pandemic disease caused by a novel coronavirus SARS-COV-2 has spread like a forest fire and affected 213 countries worldwide. WHO reported 233,136,147 confirmed cases globally and 4,771,408 death by 28 September 28, 2021. Based on our current understanding of the global outbreak, this review represents our understanding of COVID-19 and pregnancy. Therefore, the main goal for the management of COVID-19 infection during pregnancy is preventive measures and symptomatic treatment (Jean *et al.*, 2020).

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WHO reports that the use of herbal therapies is on the rise worldwide and more than 80% of people in developing countries are using traditional/complementary and alternative medicines (Simbar *et al.*, 2008). Traditional medicines (TMs) have been practised worldwide for thousands of years and it includes Unani medicine, Ayurveda, Homoeopathy, Traditional Korean medicine (TKM), Traditional Chinese medicine (TCM), and Kampo medicine. All these traditional medicines use natural compounds for the treatment of diseases. Unani (Greco-Arabic) medicine is one of the most important traditional holistic medicine dates back 2500 years, originated in Greece (Yuan *et al.*, 2016) and is based on teachings of Hippocrates, Galen and Arab physicians. It is highly possible that Greek (Greco-Arabic/ Unani) medicine, originally arrived in India with the crusade of Alexander the Great in Asia (334-323 BC). In India, it has gained official status, integrated into the national health care system and included in the Ministry of AYUSH (Nikhat and Fazil, 2020). WHO has recognized Unani medicine as an alternative healthcare system (Yuan *et al.*, 2016).

Though direct evidence is not available, some research studies on traditional medicines and/or integrated with conventional medicine proposed that they may have a direct efficacy on the virus. Unani medicine has a unique role in health promotion, prevention and management during epidemics and pandemics. Unani medicine has highlighted the concept and practices that are beneficial in flu-like epidemic diseases under *huma-i-wabaiya* and *nazla-i- wabaiya* (Rushd, 2017; Sina, 2009; Sina, 2010). The various scientific studies have confirmed that Unani/herbal drugs use in flu-like epidemics have specific immunomodulatory effects (Nikhat and Fazil, 2020) and natural compounds have an action against human coronavirus (Xian *et al.*, 2020). In this manuscript, an attempt is made to comprehend a summary of COVID-19 and pregnancy in contemporary medicine, Unani concept and practices for flu-like epidemic diseases in general and during pregnancy. Further, the traditional and Unani/herbal drugs were explored in scientific databases for effectiveness and safety for the prevention and treatment of mild symptomatic cases of COVID-19 and pregnancy.

METHODOLOGY

The methodology included five steps. In the first step research questions and problems were identified. The second step included a literature review and identifying relevant studies. The third step included literature and study selection. The fourth and fifth steps included data charting processing and summarizing the reviews respectively.

Step 1: Identifying research questions: The following questions directed this scoping review for an overview of Covid-19 and pregnancy in the contemporary era and the concept, practices and safety of Unani/herbal medicines in COVID-19 infection during pregnancy for the prevention and treatment of mild symptomatic cases.

What is the overview of COVID-19 and pregnancy in the contemporary era? What is the concept and practices for flu-like epidemics in general and during pregnancy in Unani medicine for the prevention and probable management of COVID-19 symptoms? Is evidence-based safety data available for herbal drugs/Unani medicine used in COVID-19 infection and other epidemics including respiratory diseases?

Step 2: Literature search and identifying relevant studies: We conducted a meticulous literature search in PubMed, LitCovid, Google Scholar, Science Direct, Springer, EBSCO Web of Science, and Scopus electronic databases for an overview of COVID-19 and pregnancy in the contemporary era for the most current information concerning the pandemic. Scrupulous exploration was conducted to comprehend the concept and practices of flu-like epidemics in general and related to pregnancy described in classical Unani textbooks and pharmacopoeia. The classical Unani texts viz., *The Complete Art of Medicine* (*Kāmil al-Sanā 'a al-Tibbiyya*), Canon of medicine (*Al-Qānun Fi'l Tibb*), Continens Liber (*Kitāb al-Hāwi fi'l Tibb*), *Humayait Qānun*, *Haziq, Shariah Asbab, Kitāb al-Kulliyyāt, Kitab al-Mansoori* and *Iksir-i-A'zam* were referred for concepts and practices for epidemics/flu-like epidemics in *asbab sitta daruriyya*, *nazla-i-wabaiya*, and *huma-i-wabaiya*. National Formulary of Unani Medicine (Ministry of AYUSH), Unani Pharmacopeia of India, *Bayaz Kabir*, *Qarabadeen Qadri*, *Mukhazanul Mufradat*, and other pharmacopoeia were retrieved for single drugs and compound formulations useful to treat signs and symptoms related to respiratory disorders and COVID-19 infection. Next, PubMed, Google Scholar, Ovid, Science Direct, Springer and other major scientific databases were also scrutinized for the knowledge related to the concept, practices and comprehensive scientific evaluation of the effectiveness and safety of these medicines in flu-like epidemics in general and pregnancy. The search terms/keywords were "Unani and waba", "Unani medicine and respiratory diseases", "herbs used in COVID-19", "weather and COVID-19", "Climate change and epidemics" "traditional medicine and COVID-19", "safe herbal drugs used during pregnancy", "herbs contraindicated during pregnancy", "Unani medicine and pregnancy", "COVID-19 during pregnancy and herbs", "natural compounds", "immunomodulatory herbs", "antiviral herbs", and Unani drugs useful in pregnancy and flu-like symptoms and epidemics. All articles were meticulously evaluated without any language or time restriction.

Step 3: Literature and study selection: First and second authors self-reliantly screened Unani texts and pharmacopoeia. Citation titles and abstracts were reviewed and potentially relevant articles in full were included. Authors considered all article reporting review or original research of COVID-19 and pregnancy for an overview, concepts and practices for epidemics in Unani medicine, herbal drugs contraindicated and safe during pregnancy.

Step 4: Data charting process: A data-charting in electronic form was jointly developed by the first author to determine which variables to extract. Second and third authors (MK and KR) independently extracted data and the first author (AS) continuously updated the data-charting form. We extracted the following data items: general data (author's name, title, year of publication, country); methodological data (original, review, case studies, case reports and meta-analysis/systematic reviews), discussion and conclusion. The authors also extracted and documented chemical constituents, pharmacological activities, effectiveness and safety of each herb. A total of 200 articles and textbooks were retrieved to collect the information regarding COVID-19 and pregnancy in Unani and contemporary medicine. The articles that were included in the manuscripts encompassed 31 research articles, 41 review articles and 17 textbooks.

Step 5: Summarizing review: The review was organized under the following categories:
Overview of COVID-19 and pregnancy and concept and practices of flu-like epidemics in general and related to pregnancy. Further, Traditional and Unani drugs scientific studies related to safe use in pregnancy for symptoms related to COVID-19 such as fever, sore throat, nausea and vomiting, diarrhoea, other respiratory and related symptoms were summarized.

DISCUSSION

Overview of Covid-19 infection during pregnancy in contemporary medicine

Pregnant women have a higher risk of serious illness and death from viral infections (influenza and ebola) during pandemics (Zhao *et al.*, 2020). They are not immune from the existing COVID-19 pandemic, and obstetric care will unavoidably be impacted by this pandemic (Stephen *et al.,* 2020). The incubation period ranges from 1 to 14 days, an average from 2-6 days in most patients. (Jean *et al.,* 2020).

Similarly, they are more susceptible to COVID-19 infection due to partial immune suppression status, anatomical, physiological, reproductive and endocrine adaptive changes (Liang and Acharya, 2020; Luo and Yin, 2020; Omer *et al.*, 2020, Zhao *et al.*, 2020).

Another reason for higher susceptibility to SAR-CoV-2 during pregnancy is a significant increase in angiotensin-converting enzyme (ACE)-2, the SARS-CoV-2 receptor. A substantial percentage of deaths with COVID-19 are due to dyspnea as per present statistics. In the third trimester of pregnancy, the incidence of physical dyspnea is 50–70%. Certainly, SARS-CoV-2 infection will indisputably deteriorate the degree of breathing difficulties (Zhao *et al.,* 2020). Hence, this disease may have serious consequences for pregnant women. However vertical transmission is unclear (Luo and Yin, 2020; Zhao *et al.,* 2020).

The pregnant women can generally be triaged and stratified into 1) mild disease (i.e., symptomatic with stable vital signs); 2) severe disease (i.e., resting saturated $O2 \leq 93\%$, respiration rate $\geq$ 30/min, arterial blood oxygen partial pressure/oxygen concentration $\leq$ 300 mmHg); and 3) critical disease (i.e., respiratory failure requiring mechanical ventilation or refractory hypoxaemia requiring extra-corporal membrane oxygenation and shock with organ failure) in COVID-19 disease (Omer *et al.,* 2020).

Farida *et al.,* (2020) in a systematic review summarized that 95.6%, 3.6% and 0.8% of pregnant women had mild, severe and critical illnesses respectively and out of which only one woman died. They concluded that COVID-19 infection during pregnancy has a similar clinical presentation and illness severity to non-pregnant adults. However, the potential of SARS-CoV-2 to cause severe obstetric and neonatal adverse outcomes is unknown (Luo and Yin, 2020).
The previous studies reported that SARS coronavirus infection during pregnancy may probably cause spontaneous abortion, (Omer *et al.,* 2020), intrauterine growth retardation, preterm delivery (Luo and Yin, 2020; Omer *et al.,* 2020), intrauterine death, neonatal death, premature rupture of membranes, fetal distress and fetal tachycardia in the third trimester of pregnancy (Liang and Acharya, 2020; Luo and Yin, 2020).

In COVID-19 infection, patients may have normal or reduced peripheral white blood cell count in early stages, low lymphocyte count, mild thrombocytopenia, elevated levels of liver enzymes, creatine phosphokinase and C-reactive protein may be increased. To rule out or confirm viral pneumonia a computed tomography (CT) scan of the chest without contrast should be performed in suspected cases as the risk of radiation exposure to the fetus is very small. In the majority of reported pregnancies with COVID-19 infection, radiological signs of viral pneumonia were present. A preferable and standard method for the diagnosis of SARS-COV-2 nucleic acid is real-time polymerase chain reaction (RT-PCR). COVID-19 infection can be ruled out, if the RT-PCR test taken on two consecutive occasions at least 24 hours apart is negative. If RT-PCR is not available for a diagnostic procedure, the serology test should be used. To screen out other respiratory infections, samples should also be tested for other viruses and blood culture for bacterial infection (Liang and Acharya, 2020). Lung ultrasound examination and X-ray as a diagnostic imaging tool in pregnant women with suspected COVID-19 is also useful. It is primarily a respiratory illness, therefore needs to be differentiated from other respiratory illnesses However, the significant overlap of imaging findings with other acute viral respiratory infections, imaging alone is unlikely to supplant the role of RT-PCR for the primary diagnosis of COVID-19 (Ashokka *et al.,* 2020).

SOCG guidelines for routine antepartum and intrapartum care ould be followed. (Elwood *et al.,* 2020). Pregnant women with COVID-19 pneumonia and critically ill needs management by a multidisciplinary team at a tertiary care centre. As per SOCG updated guidelines (May 14, 2020), empiric antibiotic therapy for superimposed bacterial pneumonia should be considered in women with COVID-19. The management of pneumonia includes oral amoxicillin as the first-line antibiotics for stable patients and ceftriaxone for severe disease (Elwood *et al.,* 2020). An individualized decision for delivery in a severe COVID-19-positive patient during the third trimester is required (Stephen *et al.*, 2020).

Nevertheless, there is scarce information regarding the prevention and management of infected pregnant women (Favre *et al.*, 2020; Luo and Yin, 2020). As per our knowledge, the most important apprehension of the COVID-19 pandemic is maternal and fetal safety. Pregnant women practice and maintain good personal and social hygiene, avoid crowded places, do not contact sick people, refrain from unnecessary travel and public transport. Some pregnant women could require psychological support to avoid adverse outcomes that may probably develop due to severe anxiety and depression and with any symptoms such as fever, fatigue, sore throat, cough, myalgia, or shortness of breath should pursue medical

consultation Intrapartum management includes the screening of all patients and visitors, limiting the visitors at a time of delivery, isolating confirmed cases as per the guidelines, using appropriate personal protective equipment in all areas of labour and delivery units by the health care provider, patients, and visitors, management of labour and delivery as per obstetrics indication.

Table 1. Unani formulations probably useful in prevention and management of symptoms related to flu- like epidemics and COVID-19

Sr. no.	Herbal formulation	Composition	Relevant action	Therapeutic effect	Dosage	Comments	Reference
1.	*Habb-e-Surfa*	*Asl-us-Soos* *Tukhm-e-Khubbazi* *Maghz-e-Tukhm-e-KadduSireen* *Samagh-e-Arabi* *Kateera* *Nishasta-e-Gandum* *Zafran*	Musakkin-e-sual (cough depressant)	Sual (cough)	125-250 mg	Safe (U)	National Formulary of Unani Medicine, 2006.
2.	*Habb-e-Tabasheer*	*Tabasheer* *Tukhm-e-Gaozaban* *Satt-e-Gilo* *Dana Heel Khurd* *ZaharMohra*	Mufarreh (exhilarant) Daf-e-tap (anti-pyretic) Daf-e-humudat (antacid) Musakkin (analgesic)	Hummiyat (fever) Atash-e-mufrit (thirst) Humuzat-e-meda	750-1.5 g	Safe (U)	Govt Unani Pharmacopeia, 1998; National Formulary of Unani Medicine, 2006.
3.	*Habb-e-Bukhar*	*Tabasheer* *Kanakana* *Satt-e-Gilo* *Samagh-e-Arabi*	Daf-e-humma Moarriq (diaphoretic)	Humma-e-hadda (acute fevers)	250-500 mg	Uncertain as *Kanakana* has emmenagogue property	Kabir al-Din, 2007; National Formulary of Unani Medicine, 2006.
4.	*Habb-e-Bohat-us-Saut Haad*	*Kateera* *Nishasta-e-Gandum* *Samagh-e-Arabi* *Rubb-us-Soos* *Maghz-e-Tukhm-e-Kaddu* *Maghz-e-Tukhm-e-Khiyarain*	Mulattif (demulcent)	Buhhat al-Sawt haad (hoarseness of voice) Su'al (cough)	250-500 mg	Safe (U)	National Formulary of Unani Medicine, 2006,
5.	*Habb-e-Hindi Zeeqi*	*BeeshMudabbar* *Post-e-Beekh-e-Madar* *Aab-e-Adrak*	Munaffith-i-balgham (expectorant) Dafi-i-tashannuj (antispasmodic/anticonvulsant)	Zeeq-un-Nafas (bronchial asthma)	125-250 mg	Uncertain as *Beesh* and *bekh madar* have emmenagogue and abortifacient	Kabir al-Din, 2007; National Formulary of Unani Medicine, 2006,
6.	*Habb-e-Mubarak*	*Kaifal* *Karanjwa*	Daf-e-tap (antipyretic)	Humma-e-ajamiya (fever)	1-2 g	Uncertain as *karanjwa* has emmenagogue property	Kabir al-Din, 2007; National Formulary of Unani Medicine, 2006.
7.	*Dayaqooza*	*Koknar Musallam* *Asl-us-Soos* *Gul-e-Nilofar* *Gul-e-Banafsha* *Gaozaban* *Unnab* *Sapistan*	Musakkin-e-sual (antitussive) Munaffith-i-balgham (expectorant) Muhallil-i-waram (anti-inflammatory)	Nazla-o-zukam (coryza and catarrh) Su'al (cough)	10-20 g	Uncertain as *Opium* is abortifacient	Kabir al-Din, 2007; National Formulary of Unani Medicine, 2006.
8.	*Khamira-e-AbreshamSada*	*Abresham* *Gul-e-Gaozaban* *Barg-e-Raihan* *Tukhm-e-Raihan* *Badranjboya* *Gul-e-Nilofar* *Sandal Safaid* *DarunajAqrabi* *Arq-e- Gulab*	Muqawwi-i-qalb (cardiotonic)	Khafaqan (palpitation) Karb (distress) Duf al-Qalb (cardiac weakness)	5-10 g	Safe (U)	National Formulary of Unani Medicine, 2006.
9.	*Khamira-e-Marwareed*	*Marwareed* *Tabasheer* *Sandal Safaid*	Muqawwi-e-aam (tonic)	Zof-e-qalb Zof-e-asab Khafqan	3-5 g	Safe (U), Human trial for palpitation during	Bashir *et al.*, 2019; Mustafaa *et al.*, 2001;

		Ambar Ash-hab *Arq-e-Gulab* *Arq-e-Bid-e-Mushk* *QandSafaid*		Atash-e-mufrit Zof-e-dimagh		pregnancy	National Formulary of Unani Medicine, 2006.
10.	*Khamira-e-Banafsha*	*Gul-e-Banafsha* *Aab (water)* *Qand (sugar)*	Munaffith-i-balgham Mulayyin (laxative)	Nazla Sual Qabd (constipation)	20-40 g	Safe (U)	National Formulary of Unani Medicine, 2006.
11.	*Khamira-e-Gaozaban Ambari Jawahirwala*	*Gaozaban* *Gul-e-Gaozaban* *KishneezKhushk* *Abresham* *BehmanSafaid* *Sandal Safaid* *Tukhm-e-Balango* *Tukhm-e-Raihan* *Warq-e-Nuqra* *Marwareed* *Yaqoot* *ZaharMohra* *Zumurrud* *Ambar Ash-hab*	Muqawwi-e-aam (tonic)	Zof-e-qalb (cardiac weakness) Zof-e-dimagh Karb Khafqan Malikhuliya Zof-e-asabNazla muzmin	3-5 g	Safe (U)	Bashir *et al.,* 2019; National Formulary of Unani Medicine, 2006.
12.	*Khamira-e-GaozabanSada*	*Gaozaban* *Gul-e-Gaozaban* *KishneezKhushk* *Abresham* *BehmanSafaid* *Sandal Safaid* *Tukhm-e-Balango* *Tukhm-e-Raihan* *Badranjboya*	Muqawwi-e-aam	Zof-e-qalb Zof-e-dimagh	5-10 g	Safe (U) Borage used for sedation during pregnancy in folk medicine	National Formulary of Unani Medicine, 2006; Saber *et al.*, 2019
13.	*Laooq-e-Behidana*	*Behidana* *Aspaghol* *Tukhm-e-Khatmi* *Aab-e-Kakri* *Aab-e-Anar Shireen* *Aab-e-Kaddu* *Aab-e-Barg-e-Khurfa* *Samagh-e-Arabi* *Kateera* *Maghz-e-Badam Shireen* *Tukhm-e-Khashkhaash* *Rubb-us-Soos* *ShakarTeghal*	Murattib Mubarrid (coolent)	Sual-e-yabis (dry cough) Sil (tuberculosis)	5-10 g	Safe (U)	National Formulary of Unani Medicine, 2006.
14.	*Laooq-e-Sapistan*	*Sapistan* *Unnab* *Koknar* *Asl-us-Soos* *Parsiyaoshan* *Tukhm-e-Khatmi* *Tukhm-e-Khubbazi* *Behidana* *Sheera-e-Maghz-e-Badam* *Sheera-e-Tukhm-e-Khashkhash* *Kateera* *Samagh-e-Arbi* *Rubb-us-Soos*	Munaffith-i-balgham Musakkin-e-sual	Nazla Zukam (cold and coryza) Sualmuzmin (chronic cough) Anaf-ul-anzah	10-20 g	Uncertain as *opium* and *parsiyaoshan*is present. *Parsiyaoshan*has emmenagogue property	Kabir al-Din, 2007; National Formulary of Unani Medicine, 2006.
15.	*Laooq-e-Katan*	*Loab-e-Tukhm-e-Katan* *Asl* *ShakarSurkh*	Musakkin Muhallil-e-waram Anitpyretic, Anti-inflammatory Antioxidant Immunomodulatory	Zat-ur-riyah Sual Zeeq-un-nafas (bronchial asthma) Respiratory diseases and allergies	10-20 g	Safe (U). Animal study showed safe in pregnancy.	Correia-Santos *et al.*, 2015; Jabeen *et al.*, 2014; National For mulary of Unani M edicine, 2006; Shek *et al.*, 2012

16.	*Sharbat-e-Sadar*	*Barq-e-Arusa* *Unnab* *Gaozaban* *Tukhm-e-Katan* *Badiyan* *Nankhwah* *Koknar* *Gul-e-Gaozaban* *Sapistan* *Tukhm-e-Khatmi* *Abresham* *Asl-us-Soos* *Parsiyaoshan* *Arq-e-Gaozaban* *QandSafaid*	Munzij Munaffith-i-balgham	Sual Zeeq-un-Nafas Nazla-muzmin Sil	20-40 ml	Uncertain as it contains *opium, parsiyaoshan*	Kabir al-Din, 2007; National Formulary of Unani Medicine, 2006.
17.	*Sharbat-e-Toot Siyah*	*Aab-e-Toot Syah* *QandSafaid*	Muhallil-e-waram (Anti-inflammatory) Mulattif	Bohat-us-SautHaad Warm-e-lauzatain Warm-e-hanjara (pharynigitis) Nazla Sual	20-40 ml	Safe (U) Animal experiment in diabetic pregnant rat showed no adverse effect.	Lim and Choi, 2019; National Formulary of Unani Medicine, 2006.
18.	*Sharbat-e-Unnab*	*Unnab* *Aab* *QandSafaid*	Munaffith-i-balgham Musakkin Antipyretic Expectorant	Sual Sore throat, fever, nazla, zukam,	20-60 ml	Safe (U) RCT on consumption ofJujube in pregnancy has been documented.	Govt Unani Pharmacopeia, 1998; Kelishadi *et al.*, 2016; National Formulary of Unani Medicine, 2006.
19.	*Gulqand-e-Gulab*	*Ward-e-Gul-e-Surkh Taza* *Qand Safaid*	Mulaiyin (Laxative) Muqawwi-e-meda (stomachic) Muqawwi-e-dimagh (Brain tonic) Muqawwi-e-kabid (hepatotonic) Mufarreh (Exhilarant)	Zof-e-kabid Zof-e-meda Zof-e-dimagh Qabz Sil Diq	10-30 g	Safe (U) Clinical trial of essential oil of rose in low backache during pregnancy has shown no adverse effect on pregnant women and fetus	National Formulary of Unani Medicine, 2006; Shirazi *et al.*, 2016
20.	*Tiryaq-e-Arba*	*Juntiyana* *Zarawand* *Habb-ul-Ghaar* *Murmakki* *Aslkhalis*	Daf-e-sumoom (Antidote) Daf-e-tashannuj Mufattih-e-sudad (deobstruent) Mudirr-e-bawl	Tasammum (Anti dote for animal toxins) Tashannuj Qulanj Usr-e-wiladat Tasaddud-e-Urooq istisqa	3-5 g	Used to ease the labour and to expel dead fetus (U).	Govt Unani Pharmacopeia, 1998; National Formulary of Unani Medicine, 2006.
21.	*Sikanjabeen Lemooni*	*Zof-e-Kabid* *Zof-e-Meda* *Atash-e-Mufrit* *Zof-e-Hazm* *Haiza* *Ghasiyan* *Qai* *Su-e-Hazam*	Muqawwi-e-kabid	Zof-e-meda, Zof-e-kabid, Qai, Su-e-hazam, Haiza (cholera), Atash-e-mufrit	25-50 ml	Safe (U), Human trial for nausea and vomiting during pregnancy has been documented.	Bashir *et al.*, 2019; Anjum *et al.*, 2018; Govt Unani Pharmacopeia, 1998 National Formulary of Unani Medicine, 2006.
22.	*Qairooti-e-Aarad-e-Karsana (local application)*	*Aarad-e-Karsana* *Tukhm-e-Hulba* *Kalonji* *Asl-us-Soos* *Aaqaqarha* *Mom Zard* *Rogan-e-Gul*	Muhallil-e-waram	Zat-ul-janb (pleurisy) Zat-us-sadar Zat-ul-arz Zat-ul-riya (pneumonia)	Q.S (External use)	Safe (U) Topical application	Khan, 1983; National Formulary of Unani Medicine, 2006.
23.	*Arq Ajeeb (local application)*	*Nafkh-e-Shikam* *Ghasiyan* *Qai* *Su-e-Hazm* *Waj-ul-Meda* *Is-hal* *Waj-ul-Fawad* *Haiza* *Qulanj* *Nazla*	Kasir-e-riyah (Carminative) Musakkin-e-alam (Analgesic) Anesthetic	External use for: Laza-e-hashrat Shaqiqa Suda Sual	2-5 drops	Safe (U) Thymol: Topically, it is safe and not associated with increased risk of birth defect.' Camphor: No increase risk of congenital anomalies in	National Formulary of Unani Medicine, 2006; Alsaad *et al.*, 2015.

		Zukam				animal studies. No adverse effect in human. Menthol: Topically,it is safe. There is no teratogenic effect in animals.	
24.	*Tiryaq-e-Afayee*	*SibrZard Mur Makki Zafran*	Daf-e-sumoom Man-e-asarat-e-waba (Anti-epidemic)	Humma-e-wabaiya Laza-e-hashrat	1-2 g	Uncertain as sibr is emmenagogue orally.	National Formulary of Unani Medicine, 2006; Razi, 2008; Sina, 2010

Table 2. Plant material used in Unani medicine during pregnancy for prevention and management of symptoms related to flu-like epidemics and COVID-19

S. no.	Unani name	Botanical name	Part used	Relevant actions	Indications/ Rationale for use	Active Phytoconstituents	Route	Comments	Reference of safety
1	*Anar Syn. Roomaan, Gulnaar, Gulnaar Farsi, Pomegranate*	*Punica granatum* Linn	powdered flower fresh juice of fruit	antiviral, antiseptic, parasiticide, antipyretic antimicrobial	asthma, bronchosis, cough, malaria, sore throat, anorexia diarrhoea, dyspepsia, inflammations of the stomach, palpitation, excessive thirst and fevers.	malvidin pentose glycoside; proanthocyanidins	oral	Safe (u) clinical trial reported no health hazards in therapeutic doses in pregnant women for nausea and vomiting a clinical trial in preeclampsia in pregnant women is documented	Abdol Hosseini *et al.*, 2016; Bashir *et al.*, 2019; Duke, 2002; Kabir al-Din, 2007; Khare, 2007; Kusumawati, 2016
2	*Asl-us-soos Syn. Mulethi. Rubb-us-soos (extract), Liquorice*	*Glycyrrhiza glabra* Linn.	root	demulcent, expectorant, antiallergic, anti-inflammatory, spasmolytic, estrogenic, emmenagogue, antidiabetic	catarrh of the upper respiratory tract bronchitis, dry cough, respiratory infections, catarrh, tuberculosis, abdominal pain	glycyrrhizin glycyrrhetinic acid, isoflavonoids, chalcones, coumarins, triterpenoids and sterols, lignans, amino acids, amines, gums and volatile oils.	oral	Safe in therapeutic dose use with caution contraindicated in high dose (>500 mg/week)	Duke, 2002; Kabir al-Din, 2007; Kennedy *et al.*, 2016; Khare, 2007
3	*Banafashaa Syn. Banafsaj, Kakosh, Fareer, Sweet Violet*	*Viola odorata* Linn.	flower, root	expectorant, anti-inflammatory, diaphoretic, antipyretic, diuretic, antioxidant, antimicrobial, antiasthmatic, anti-hiv	catarrhal and pulmonary affections, diseases of liver and intestines	glucose, delphinidin, rhamnose and pcoumaric acid, tocopherol, anthocyanin, violanin chloride, anthocyanin, total flavonoids, rutoside, mucilage, friedelin and beta-sitosterol.	oral	Use with caution. use in folk medicine,no adverse effect reported	Duke, 2002; Jabinand Aman 2010; Jasim *et al*., 2018; Kabir al-Din, 2007; Kennedy *et al.*, 2016; Khare, 2007
4	*Bihi Syn. Bihidaanaa, Quince*	*Cydonia oblonga* Mill	fruit, seeds	fruit pulp and seeds: soothing, demulcent leaf, bud and bark: astringent fruit: expectorant, anti-influenza, antioxidant,	diarrhoea, dysentery catarrh, headache, pulmonosis	seed kernel: a glycoside amygdalin, tannin, mucilage, fatty oil fruit: pectin, ionone glycosides,	oral	Safe clinical trial in pregnant women for nausea and vomiting no side effects reported	Abdol Hosseini *et al.*, 2016; Ahmed *et al.*, 2017; Bashir *et al.*, 2019; Duke, 2002;

				antimicrobial		octadienoic acid, thiamine, riboflavin, nicotinic acid, vitamin b6, inositol, pantothenic acid, folic acid and biotin			Hamauzu *et al.*, 2005; Kabir al-Din, 2007; Khare, 2007; Shakeri *et al.*, 2018; Wang *et al.*, 2006
5	*Gulab Syn. Gul-e-Surkh, Vard, Varde-Ahmar Stamens—Zard-e-Vard Fruit—Dalik, Samar-ul-Vard, Smar-e-Gul*	Rosa damascene Herrm	petals, distillate of petals	flower buds—astringent, expectorant, laxative, antioxidant stamens and fruits—astringent. petals—gulkand (a confection in sugar)—laxative, anti-inflammatory rose water—cooling, refrigerant, antiseptic, anti-inflammatory	used as a cardiac tonic and aperients, sore throat and tonsillitis, a remedy for skin irritation, for soreeyes	quercetin, kaempferol and cyanidin. lycopene, rubixanthin, zeaxanthin, xanthophyll and taraxanthin flowers: essential oil with citronellol, nerol, geraniol, beta-phenylethanol and its glucoside, eugenol and methyl eugenol sugars	oral/spray	Safe (u) clinical trial of essential oil in low backache during pregnancy	Bashir *et al.*, 2019; Hashem Dabaghian *et al.*, 2015; Duke, 2002 Kabir al-Din, 2007; Khare, 2007; Razi, 1991; Shirazi *et al.*, 2016
6	*Gaozabaan Syn. Borage, Cow's Tongue Plant*	Borago officinalis Linn.	all parts	anti-inflammatory, antipyretic, expectorant, demulcent, emollient, restorative, nervine tonic. febrifuge, refreshing & restorative	alleviate pulmonary affections, cough, catarrh, fever, pharyngosis, pulmonosis, stress, mental exhaustion, and depression	gamma-linoleic acid and linoleic acid. borage oil predominant unsaturated pyrrolizidine alkaloids-lycopsamineand supindineviridiflorate cholin, glucose, fructose, amino acids, tannin, protein, oil.	oral	Safe (u) use in folk medicine during pregnancy	Duke, 2002; Kabir al-Din, 2007; Khare, 2007; Saber *et al.*, 2019
7	*Habb-ul-Aas, Syn. Muurad, Muurad-daan, Myrtle*	Myrtuscommunis Linn.	fruit	antiseptic, antimicrobial, antiparasitic, analgesic, antibacterial, insecticidal, bronchosecretolytic, pectoral, antiviral hepato-protective neuroprotective antioxidants	cough, acute and chronic respiratory tract infections fever, bronchosis, diarrhea, headache, pharyngosis, pulmonosis, sinusosis	tannins, flavonoids, coumarins, essential oil, fixed oil, fibres, sugars, citric acid, malic acid	oral	Safe (u) no adverse reactions noted in proper dose	Duke, 2002; Kabir al-Din, 2007; Khare, 2007; Masoudi *et al.*, 2016, Sumbul *et al.*, 2011
8	*Halela Syn. Harad, Halelaasiyaah, Halelaazard, HalelaaKaabuli (varieties).*	TerminaliachebulaRetz	fruit	anti-bacterial, gentle purgative,astringent, laxative, stomachic, anti-bilious, alterative. antioxidant	cough and bronchial asthma, intermittent fevers, chronicfevers, flatulence, constipation, diarrhoea, dysentery,cyst,digestive disorders, vomiting, enlarged liver and spleen	shikimic, gallic, triacontanoic and palmitic acids beta-sitosterol, daucosterol,triethylester of chebulicacid and ethyl ester of gallic acid; triterpene, chebupentol, arjungenin, terminoic acid, arjunolic acid,	oral/gargle	Safe	Duke, 2002 Kabir al-Din, 2007; Khare, 2007;

					andformetabolicharmony	phloroglucinol and pyrogallol			
9	*Khaksi Syn. Khuubkalaan*	Sisymbriumirio Linn.	seeds	expectorant, restorative, rubefacient, antibacterial, analgesic, antipyretic, antimicrobial, antioxidant	asthma, throat and chest infections	iso-rhamnetin, linolenic and oleic acids, also erucic, palmitic and stearic acids, alkaloids, organic acids, tannins, glycosides, saponins, coumarins flavonoids.	oral	Safe (u) the plant is used during pregnancy. It is highly safe since substances possessing ld50 higher than 50 mg kgare non-toxic. Used for cervical priming during late pregnancy	Al-Jabbar, 2011 Duke, 2002 Kabir al-Din, 2007; Khare, 2007; Kordi *et al.*, 2017; Saber *et al.*, 2019
10	*Lahsun Syn. Seer, Garlic*	Allium sativum Linn.	cloves/ bulb	antiviral, antioxidant, cardiotonic, hepatoprotective, antipyretic, immunostimulant, antibiotic, bacteriostatic	upper respiratory tract infections and catarrhal conditions, catarrh, cold, bronchiectasis, bronchosis	sulphurcontaining amino acids known as alliins (alkylcysteine sulfoxides) particularly methylalliin andpentylalliin enzyme alliinase monosulfide	oral/spray	Safe (u) garlic tablet in nulliparous pregnants at high risk of preeclampsia was studied. Intakes of garlic and dried fruits are associated with lower risk of spontaneous preterm delivery.	Ahmed *et al.*, 2017; Duke, 2002; Kabir al-Din, 2007; Kennedy *et al.*, 2016; Khare, 2007;Myhre *et al.*, 2013; Ziaei *et al.*, 2001
11	*Lemon Syn. Utraj, Nimbu*	Citrus limon Linn.	fruit	fruit: antiscorbutic, carminative, stomachic, anti-histaminic, antibacterial. leaves andstems-antibacterial	coughs, colds, influenza and onset of fever, hiccoughs, biliousness. fruit juice—externally for ringworm (mixed with salt), erysipelas, also in the treatment of leprosy and white spots.	flavonoids (flavanones, flavones, 3-hydroxyflavylium) and limonoids, antiscorbutic vitamin, alpha- and beta-pinenes, alpha-terpinene and citral,	oral	Safe (u) RCT in pregnant women for nausea and vomiting no side effects reported	Duke, 2002; Kennedy *et al.*, 2016; Kabir al-Din, 2007; Khare, 2007; Abdol Hosseini *et al.*, 2017
12	*Pudina Syn. Pudinaa, Nanaa, PudinaaKohi*	Peppermint, Mentha piperata Linn. Spearmint garden mint =Mentha spicata Linn.	flowers, leaves	analgesic, antipyretic, antiseptic, antispasmodic, decongestant, antiviral carminative, stimulant, antispasmodic, antiemetic, diaphoretic, antiseptic	asthma, bronchosis, catarrh, coryza, cough, headache, pneumonia, tracheobronchitis, bronchosis, cold, cough, fever, headache	carvone, limonene, flavonoids-diosmin and diosmetin. caffeic acid derivatives-rosmarinicacidinthevolatile oil	oral	Safe (u) Human trial in pregnant women documented as safe	Ahmed *et al.*, 2017; Duke, 2002; Kabir al-Din, 2007; Kennedy *et al.*, 2016; Khare, 2007
13	*Sapistan*	Cordia myxaRoxb. Cordia dichotomaF	fruit/ berry, bark, kernel	antimicrobial, antioxidant, immunomodulator astringent,	diseases of the chest and urinary passage, fevers,	alkaloid, flavonoid (rutin, rutoside, hesperidin), phenolic	oral	Safe(u)	Al-Snafi-2016; Duke, 2002; Gupta and

		orst		demulcent, expectorant, mucilaginous antipyretic analgesic, anti-inflammatory	decoction used in cough and cold.	compounds, saponins terpenes			Kaur, 2015; Kabir al-Din, 2007; Khare, 2007;
14	*Sibr Syn. Gheekwaar, Elwaa*, Aloe vera	Aloe barbadensis Mill.	dried juice of leaves, gel/ pulp	vulnerary[4], anti-viral[4], anti-inflammatory[4] astrongpurgative, digestive tonic, antiviral, immunomodulator, reputed abortifacient actions(on internal ue)	asthma, bronchosis	anthraquinone glycosides, carboxypeptidaseandsalicylate components, c-glycosyl chromone,	fumigation/topical	Safe for local use	Duke, 2002; Kennedy *et al.*, 2016; Kabir al-Din, 2007; Khare, 2007; Ahmed *et al.*, 2017
15	*Tabasheer Syn. QasabBamboo manna*	Bambusaar undinaceae Roxb.	manna (resin/exudate)	pectoral, expectorant, carminative, cooling, tonic antimicrobial, antioxidant	chest diseases, cough asthma, debilitating diseases, diarrhoea	alkaloids, phenols, terpenoids, tannin	oral	Safe (u)	Bashir *et al.*, 2019; Duke, 2002; Kabir al-Din, 2007; Khare, 2007; Owolabi and Lajide, 2015
16	*Tamarhindi Syn. Amli, Amlikaa*	Tamarindus indica Linn.	pulp of fruit	analgesic, anti-inflammatory, pulp of fruit: digestive, carminative, laxative, antiscorbutic antimicrobial antiviral antipyretic antioxidant	febrile diseases, bilious disorder, as a gargle in sore throat asthma diarrhoea constipation	fruits: tartaric acid, malic acid fruit pulp: amino acids-serine, beta-alanine, proline, pipecolinic acid,phenylalanineand leucine bitter principle, tamarindienal, isolated from the fruit pulp	oral	Safe, use in nausea and vomiting during pregnancy. There are no reported side effects for using tamarhindi during pregnancy	Hashem Dabaghian*et al.*, 2015; Duke, 2002; Ebifa-Othiena *et al.*, 2017; Havinga *et al.*, 2009. Kabir al-Din, 2007; Khare, 2007;
17	*Toot siyah Syn. TuutSiyaah*	*Morus nigra* L	fruit/ leaves	anti-inflammatory, antimicrobial berries and root bark- mild laxative, refrigerant, anti-inflammatory, emollient, diaphoretic. anti-hyperlipidemic and anti-atherosclerotic,neuroprotective hepatoprotective gastroprotective cardioprotective antioxidant antiviral (hiv) antidiarrheal	respiratory catarrh, convalescence, sore throat, dyspepsia and melancholia. as gargle in inflammations of the throat.	fruit acids: malic, citric, ascorbic acid and flavonoids-rutin saponin, alkaloid, phenolic compounds-anthocyanin	oral	Safe Animal trials proved no toxic effect.	Duke, 2002; Khare, 2007; Kabir al-Din, 2007; Lim and Choi, 2019
18	*Turanjabeen Syn. Jawaansaa*	AlhagipseudalhagiBieb	resinous exudates from fruit and stem	anti-microbial, anti-oxidant, hepatoprotective, anti-pyretic laxative, antibilious, diuretic,	leaves- used for fever, headache, rheumatism. flowers—blood	flavonoids, tannins, sterols, triterpenes, saponins andanthroquinones, proanthocyanidi	oral	Safe (u) there are no reported side effects for using taranjabin during	Hashem Dabaghian *et al.*, 2015; Duke, 2002; Kabir al-Din, 2007;

				diaphoretic, expectorant., expectorant, antiemetic, laxative	coagulant, used for piles.	ns		pregnancy	Khare, 2007; Rushd, 1987
19	*Unnnab Syn. Indian Jujube*	Ziziphus jujube Mill	fruit, seeds	fruit: a nourishing, tonic, emollient, antitussive, anti-influenza, antiallergic, digestive, cardiotonic expectorant	seed: dry cough, vomiting	sisyphus saponins; jujubosides, zizybeosides, zizyvyosides, pentacyclic triterpenoid flavonoids: naringenin glycosides, vomifoloil and roseoside	oral	Safe (u) RCT on consumption of jujube in pregnancy has been documented.	Bashir *et al.*, 2019; Duke, 2002 Kabir al-Din, 2007; Kelishadi *et al.*, 2016; Khare, 2007
20	*Zaafran Syn. Saffron, Crocus*	Crocus sativus L.	stigma and style	expectorant, antioxidant, antiseptic, nervine, neuroprotective, stomachic, diaphoretic	dry cough, whooping cough, bronchitis, migraine,chronicsinusitis	crocin, picrocrocin, crocetin, carotenoids and riboflavin, thiamine, mangi-crocin, antioxidants	oral		Duke, 2002; Kabir al-Din, 2007; Khare, 2007
21	*Zanjabeel, Ginger*	*Zingiber officinalis* Linn	rhizome	antiviral, antirhinoviral, antioxidant, analgesic, antiallergic, antibacterial, anti-inflammatory, antipyretic, antiseptic, antispasmodic, antithrombic, antitussive, anxiolytic, cardiotonic, cox-2 inhibitor, decongestant, expectorant, immunostimulant antiemetic,	irritable bowel and diarrhoea, colds and influenza pregnancy associated nausea and vomiting catarrh, sore throat, cough, fever, cold, headache, asthma, vomiting pharyngosis, backache	monoterpenes, diterpenes, curcumene, gingerols, phenolic & ketone derivatives, diaryl heptenones, gingesulphonic acid and monoacyldigalactosyl glycerols.	oral	Safe (u) a systematic review and metanalysis has proven effective in nausea and vomiting in pregnancy	Ahmed *et al.*, 2017 Duke, 2002; Kabir al-Din, 2007; Kennedy *et al.*, 2016; Khare, 2007; Vilgoen *et al.*, 2014

Unani concept and practices for epidemics/flu-like epidemic diseases in general and related to pregnancy

At ancient times when Unani physicians could not state the exact cause of illness, the cause of patients deteriorating health was attributed to something in the air or water. They knew reservoirs, route of transmission, and potential causes of infections turning into epidemics. Despite the nonexistence of modern technology to establish the precise cause of an illness, physicians consistently agreed that when the body's inner healing power was diminished, it provided the substrate for viruses, bacteria and fungus to take hold. This healing power is referred to as *quwwate mudabira badan* (Physis) in Unani philosophy.

COVID-19 infection is a new disease. It affects both non-pregnant and pregnant women. In this context, direct evidence is not available in Unani literature. However, we explored the Unani textbooks for the concepts and practices for epidemics/flu-like epidemics in general and related to pregnancy in the chapters '*asbab sitta daruriyya'*, '*nazla-i-wabaiya*', 'weather, seasonal changes and epidemics', and '*huma-i-wabaiya*' and also on the symptoms-based diagnosis of COVID-19 infection. In Unani medicine, the epidemic is referred to as the *waba*.

Role of *asbab sitta daruriyya*: Unani medicine recognizes the influence of the environment and surrounding on health and lays great emphasis on the maintenance of proper eco-balance as well as pure water, food and air. As aforementioned the six essential prerequisite factors (*asbab sitta daruriyya*) should be in proper balance and whenever there is an imbalance in these factors, it potentiates diseases in humans. A good Unani physician is supposed to consider all factors before reaching a diagnosis (Ansari *et al.*, 2010).

Role of climate/weather change leading to epidemics and pandemics: Unani physicians have given great emphasis on

the role of climate/weather change in causing epidemics and pandemics. Unani physicians have given utmost importance to air/weather and the direction of winds (Razi, 2008; Rushd, 2017; Sina, 2010). Majūsī, states if southern winds are substituted by northern winds, then numerous catarrhal illnesses will occur (Majūsī, 2010). Ibn Rushd and other Unani physicians opined that usually epidemics spread in the autumn season, particularly if the preceding summer season was humid, and the wind is still (Razi, 2001; Rushd, 2017). Zakariya said that epidemics are more common when the air is warm and damp. The natural state of air change/climate change makes the community more susceptible to respiratory infections. He emphasized the fact that the patients of epidemics would have a common history and symptoms such as place, food, drink or travel' (Razi, 2008). Unani physicians claimed that unexpected growth of outbreaks of animal attacks, frequent eclipses and unwanted weather change leads to epidemics (Khan, 2011; Majūsī, 2010; Sina, 2009). It has been observed that during COVID-19 pandemics enormous climate change was noted in India like the Amphan cyclone, frequent solar eclipses, and locust attacks in various states of India.

One of the studies suggested a possible relationship between some air pollutants and SARS-CoV-2 infection rates. Both long-term and short-term exposures to the higher concentrations of air pollutants is potentially related to a higher incidence of respiratory infections caused by human pathogens (Ricco *et al.,* 2020). Other published manuscripts also showed a correlation between infectious diseases, COVID-19 and climate changes (Wang *et al.,* 2020; Wu *et al.,* 2020).

Aetiopathogenesis of infectious disease and epidemic: The pathogenesis of infectious disease/epidemic is correlated to weather/air in Unani medicine. *Hawa'* (air) present in the environment and atmosphere is a component for the body and *ruh* (vital spirit). Ibn Abbas Majūsī, (d. 994 A.D.) elaborates that whenever disequilibrium occurs in the substance of the air, pollution and putrefaction take place in *maddah* (substance) and its quality changes, causing plenty of *a'rad*-*radiyah* (symptoms) and diseases in human beings. He further states that *waba* (epidemic) outbreaks occur in the places where the natural state of air changes and it leads to *hummiyat harrah* (hot and harmful fevers), cholera, plague and other dangerous diseases. It not only affects humans but also animals. Inhalation of infected/polluted air by an individual quickly transforms the *mizaj* (temperament) of an individual and thus causes grave and deadly diseases (Ansari *et al.,* 2010; Majūsī, 2010). These are *khilt ghair tabi* (imbalance of the humours) born inside and invasion of foreign agents/contagion that affects the *akhlat* (humours). The cause of infectious and epidemic diseases are foreign agents that affect *akhlat, hararat-i-ghariza* (innate heat) and vital organs such as the heart and other organs (Khan, 1981). The same concept has been described by other physicians (Razi, 2008; Samarqandi, 2009; Sina 2009). Because of the proximity to the lungs, the airstrikes the humour in the heart easily (Khan, 1981; Rushd, 2017; Samarqandi, 2009; Sina, 2009). However, the epidemics spread through other sources also such as contact, and in these conditions, other organs would easily get affected (Samarqandi, 2009). Unani scholars explain that only susceptible individuals are affected by epidemics and not all individuals (Rushd, 2017; Sina, 2009).

Kabiruddin (2009) discussed *nazla–i-wabaiya* (flu-like epidemic) and *huma-i-wabaiya* (fever in the epidemic) (Samarqandi, 2009). Ajmal and other Unani scholars in their compilations described that plague, cholera and other diseases may outbreak and causes fatal epidemics. *Nazla-i-wabaiya* is an airborne disease and usually occurs during the winter season. The disease outbreaks in one area and spread to other places causing epidemic and pandemic infection (Khan, 1983; Majūsī, 2010). Further, children and the elderly are more prone to epidemics compared to younger individuals (Khan, 1983).

Huma-i-wabaiya: Ibne-Sina (2009) in his treatise '*Hummaiyat Qanun'* has explained that *huma-i-wabaiya* is a severe fatal fever that occurs due to *fasid* (outbreak) and *mutaffin* (infection) matter. *Waba* is the quick spread of disease to a huge number of people in a given population within a brief period. He further describes, '*radi bukharat* (contaminated aerosol) could be spread by the dead bodies of people dying due to a fatal epidemic or in the war that is not properly incinerated or buried. This *radi bukharat* may contaminate the pure air. This shows that Ibne-Sina and other Unani scholars had acquaintance with *radi bukharat*/microbes present in the body even after death, which might perhaps infect others (Khan, 2011; Rushd, 2017; Sina, 2009). Unani scholars said that air and water are the primary vehicles for transporting foreign agents (*mufsid-hawa'i* and *mufsid-i-ardi*) into the human body and cause diseases (Khan, 1981; Khan, 2011; Sina, 2009). The causative agents of epidemic disease in humans as per conventional medicine are foreign agents (bacteria, virus and other pathogens) that enter through air, food and water. Hence, the Unani concepts are probably correlated with conventional medicine.

Clinical presentation: Unani scholars state that the *nazla-i-wabaiya* is associated with fever, sore throat, sneezing, fatigue, vomiting, dry cough, chest pain, shortness of breath, loss of appetite and nasal irritation. Other symptoms such as cough, diarrhoea, and delirium may be present. They also stated that the prognosis is worsened, if pleurisy and pneumonia develop (Khan, 1983; Samarqandi, 2009). Ibn Nafees states epidemics fevers have *awarizate shadeedah* (severe complications) such as shortness of breath, etc (Rushd, 2017). If fever is of mild grade, the affected individual may not have *ghalaba su'-i-mizaj* (predominance of distemperament), whereas in *su-i-mizaj mukhatalif* the clinical features would be severe (Rushd, 2017; Samarqandi, 2009). Khan (1983) also mentioned that if symptoms are mild with no other comorbidities then within one week the patient would be relieved of the symptoms.

A study on seven pregnant women with COVID-19 pneumonia showed that the onset symptoms were similar to those reported in non-pregnant adults with COVID-19 (Luo and Yin, 2020). Other studies also reported that so far, the clinical features and severity of COVID-19 is similar between pregnant and non-pregnant women (Farida *et al.,* 2020; Omer *et al.,* 2020). In this context, the Unani texts have highlighted the symptoms in general, which include non-pregnant and pregnant women as well.

Effect of epidemics during pregnancy: Hippocrates claimed that weather/climate change leads to change in air quality and change in direction of wind usually causes abortion in a pregnant woman as mentioned by Rushd (2017). Razi (2008) also mentioned that climate change may potentiate abortions, preterm labour, intrauterine growth retardation, neonatal death or may lead to child morbidities. Galen quotes seasonal changes and changes in direction of North winds leading to abortion. Razi (2001) has mentioned that a high fever also leads to abortion. Though evidence is not available regarding the effect of novel COVID-19 infection on pregnancy outcome. However, previous pandemics related to SARS, MERS and other flu-like epidemics have shown adverse outcomes on pregnancy such as abortion, preterm, intrauterine growth retardation, neonatal death and perinatal mortality (Liang and Acharya, 2020; Luo and Yin, 2020; Omer *et al.,* 2020). A study reported that COVID-19 infection during pregnancy is probably not associated with poor maternal or perinatal outcomes. However, they concluded that clinical manifestations and outcomes of COVID-19 infection during pregnancy remain limited and fragmented (Farida *et al.,* 2020). Another study conducted in 54 pregnant women with COVID-19 confirmed and suspected cases reported that COVID-19 and pregnancy were connected with maternal morbidity and preterm birth (Sentilhes *et al.,* 2020).

Probable role of Unani medicine for the prevention and management of epidemics with special reference to COVID-19 infection

Management of Covid-19 infection in general and pregnancy includes both prevention and treatment depending on the severity of illness. To date, no medications or vaccines are approved to prevent or treat COVID-19 during pregnancy. Thus, the execution of preventive measures is imperative to avoid further spread (Zhao *et al.,* 2020). The preventive measures and management are similar for non-pregnant and pregnant women. However, while advising conventional and alternative medicine, healthcare workers should know about the safety of drugs useful in infection during pregnancy.

As per Unani medicine, the management for infectious and epidemic diseases includes

- General preventive measures: The general preventive measures include prevention of the spread of infection and anti-septic measures and maintenance of hygiene
- To normalize the humours, and treat the symptoms
- Promotion of general health, following *asbab sitta daruriya* and use of *advia tiryaqiyah* and *fad-e-zaher* (antidote) for protection from infection and epidemics.
- To protect the *hararate gharidhiyah* (vital heat) and use of cardiotonics to tone up the heart and tonic drugs for other vital organs (Khan, 1981).

Preventive measures

- General measures

a) To prevent the spread of infection, Samarqandi (2009), Razi (2008) and other eminent scholars have advised general measures such as to avoid travelling from an epidemic area to other places (quarantine, isolation and physical distancing). They also advised that in unavoidable circumstances, an individual is recommended to stay at a well-ventilated place in spacious areas, thereby decreasing the probability of getting infected. Contact transmission through fomites is possible, thus care should be taken in properly managing and disposing of the same. Care providers, family members of the patient as well as healthcare workers should take due precautions. The same is advocated in the existing time.

In epidemics, it is also advised to avoid alcohol, excessive intercourse, and excessive sleep. (Razi, 2008). Razi (2008) and Sina (2009) stated that individuals who remain physically active and exercise regularly have a lesser susceptibility to epidemic diseases. Khan (2011) opined to avoid items that cause cold and coryza in *nazla-i-wabaiya*. He also advised that as a preventive measure to protect oneself against flu-like epidemics, one should drink tea daily, eat less, avoid constipation, stay in a well-ventilated place, and wear clean clothes.

b) **Transmission-based precautions:** Razi (1991) advised that to avoid airborne infections, by adopting transmission-based precautions such as when interacting with a patient, utmost care must be taken that the air currents may not be directed from a patient to a healthy individual. Further, the causes that lead to inhaling excessive air should also be avoided. He also mentioned cough etiquettes that the patient should face away from a healthy individual while sneezing, coughing, or talking, to prevent droplet transmission and airborne infections. This is noteworthy that the preventive measures advised in existing times have been followed from ancient times as per the knowledge represented in classical Unani texts and other traditional medicine for infection spread and epidemics.

c) **Physical and mental Health:** Unani scholars have advised avoiding unnecessary physical exertion during epidemics (Razi, 2008; Sina, 2009). To maintain mental and psychological health, it is advocated to stay happy and to avoid stress, fear, depression and anger (Khan, 2011). As per the Unani advisory guidelines certain Unani drugs such as *sa'd koofi* (*Cyperus rotundus*), *ood*

saleeb (*Paeonia emodi*) and *jadwar* (*Delphinium denudatum*) would be beneficial to relieve stress (Unani guidelines, Ministry of AYUSH, 2020). A study reported that the psychological impact and apprehension of the COVID-19 epidemic appear severe in the first trimester of pregnancy during the outbreak. Using their findings, they suggested, "*to formulate psychological interventions to improve mental health and psychological resilience during the COVID-19 epidemic*" (Saccone *et al.*, 2020).

- **Control of environment:** Regarding the infection prevention and control practices, Unani scholars have mentioned maintaining air and natural ventilation, environmental cleaning and sanitation, safe water and food to prevent any infections and epidemics. The same has been suggested in infection control practices in National and International guidelines.
  - **a) Air and natural ventilation:** Hippocrates claimed to give utmost importance to air changes (Razi, 2008). Rushd is advised to stay in properly ventilated places with optimal temperature, neither too warm nor too damp (Rushd, 2017). Razi (2008) has recommended staying at a well-ventilated and spacious place if the possible distance from the low ground (hilly areas). Further, rooms should have large windows and doors and for good ventilation, large rooms may have many windows placed oppositely for cross ventilation. For natural wind flow, he advised the position of doors and windows should face to East-West as the airflow is better in this direction and the warmth of sunrays make the air light and gentle. He also states that for natural ventilation, in warm places, the door should open to the North and in damp places, the door should open to the East.

    As per national guidelines, India (2020), ventilation can reduce the risk of infection through dilution and removal of infectious particles through air exchange. Improved ventilation in health care facilities is essential in preventing the transmission of tuberculosis and other airborne infections. Currently, natural, mechanical and hybrid ventilation systems are followed for ventilation. National guidelines described that "*simple natural ventilation can be enhanced by maximizing the size of the windows, opening up fixed window panes and locating windows on opposite walls*". In Indian culture, Vastu is given great preference for building houses for natural ventilation.
  - **b) Environmental cleaning and sanitation:** Unani physicians gave great emphasis on environmental cleaning and sanitation for infection prevention and control practices to prevent epidemics as most of the epidemic diseases are airborne and spread by contact transmission. The environment is the prime medium that facilitates the spread of infections. Before the contemporary era of chemical-based air sanitisers, Unani physicians advocated for fumigation and spray of fragrant medicinal herbs for environment cleaning and disinfecting the air and surrounding from the contaminants (Nikhat and Fazil, 2020). At the time of epidemics, daily sweeping/mopping of the house and spraying with diluted vinegar and asafoetida has a clearing effect on microbes and also offers a soothing aroma (Razi, 2008; Sina, 2009). Vinegar implies the one made from sugarcane (*Saccharum officinarum* L) if otherwise specified as per Unani text (Nikhat and Fazil, 2020).

    Fumigation and spraying for prevention: Unani scholars advocated the use of fragrant drugs for fumigation in epidemics (Razi 2008, Rushd 2017). For example, *qust* (*Saussurea costus*) (Rushd, 2017), *amber* (*Liquid ambar acalycina*), camphor, honey, *sandal, ushna, za'fran* (*Crocus sativus* L.), *aabnoos* (*Diospyros ebenum*), *mushk* (*Moschus moschiferus* L.), *waj*, *abhal* (*Juniperus communis* L.), olive gum, etc (Razi 2008; Sina, 2009). Razi (2008) specifically mentioned that some drugs used for fumigation have warmth or astringent or cold effects to prevent infection and destroy the contagious agents. For example, some drugs are useful to purify warm and dry environments such as *loban* (*Styrax benzoides*), *sandroos* (*Hymenaea verrucosa*), *kundur* (*Boswellia serrat*a), *murr* (*Commiphora myrrha* Nees) *mastagi* (*Pistacia lentiscus* L.), *sibr* (Aloe vera L.), etc. These drugs produce warmth as they have warm temperament (*harr mizaj*) and also remove bad odour. Astringent drugs, for instance, *turfa* and *saad* cleanse intense moist air. Warm and light drugs such as *zanjabeel* (*Zingiber officinale* Roscoe), purify heavy air. These drugs eliminate bad odour, moderate the environment and correct the infection. He has advised fumigating quarterly, at sunrise, noon, sunset and midnight. He also advised that the aforementioned drugs could be used orally to prevent infection. Spraying of *arq-e-Gulab* (*Rosa damascene* Herrm.) (Rushd, 2017) or vinegar of onion, garlic on the walls and curtains (Khan, 2011) at home prevents epidemics. Fumigation with camphor and sandal (*Santalum album* L.) is also advisable if the air smells foul (Razi, 1991; Rushd, 2017).

    In *huma-i-wabaiya*, Ibn-Sina advised to keep the house/place cool by using *barid tadabir* such as cold aromatic herbs like *gul banafsha* (*Viola adorata*), *nilofer*, and *bade mushk* where the epidemic has spread. Frequent spraying of arq-e-*gulab, arq-e-bed mushk* and *arq-e-niloufer* is also useful to keep the place cool and to prevent infection (Sina, 2009). Gilani advised the use of *sibr* orally or as fumigant or spray in epidemics to prevent infection (Khan,

2011). In this context, the aforementioned Unani drugs used for fumigation have insecticidal, acaricidal, insect repellant and antimicrobial activities as they have various phytoconstituents such as essential oils, volatile oils, diterpenoids, terpenes, triterpenoids, and salicylaldehye. However, we could not find any clinical trials on the health effects of herbal fumigants (Nikhat and Fazil, 2020). In classical texts drugs such as *sandal, gul surkh, ood, zafran, zanjabeel,* and *mastagi* are in use during pregnancy for different ailments. Few clinical studies are published regarding the safe use of these drugs during pregnancy for different ailments (Abdolhosseine *et al.,* 2016; Al-Qamari, 2008; Bashir *et al.,* 2019; Majusi, 2010; Vilgoen *et al.,* 2014). The aforementioned drugs useful for fumigation could also be used orally to prevent infection (Razi, 2008). Few clinical studies are published regarding the safe use of these drugs during pregnancy for different ailments summarized in Tables 1 and 2. Hence, these drugs could be used safely during pregnancy for fumigation and spraying in epidemics and pandemics such as COVID-19 pandemics. Fumigation has an extensive history of cultural use and its significance cannot be deprived abruptly. However, research on the health effects of fumigation, along with quality control of drugs is the need of the hour in general and related to pregnancy. Further, herbal drugs may potentially provide a cost-effective and safer alternative to chemical disinfectants (Bhatwalkar *et al.*, 2019)

Health-promoting drugs for prevention: Unani scholars gave particular emphasis on the host defences system (Rushd, 2017; Samaraqandi, 2009). In *nazla-i-wabaiya* for prevention, Khan (1983) advised *qurs mullaiyan* two tablets with warm water per oral at bedtime to cleanse the intestine by laxative effect, followed by *joshanda* (decoction) of *luab behidana* 3g, *unnab* 5 pieces, and *sapistaan* 9 pieces with *sharbat banafsha* 20 g morning and evening. Regarding the use of *qurs mullaiyan* its use in pregnant women is uncertain as safety data is unavailable (Khan, 1983). In place of *qurs mullaiyan, gulkhand, sharbat ward, gul surkh, unnab, halela, maghz khayair shamber,* and *khamira banafsha* could be used as a laxative during pregnancy as they are safe during pregnancy (Samarqandi, 2009). Razi (2008) advocated the use of vinegar and water with *gil armani, gul surkh* and *shikanjabeen* regularly to prevent from epidemics. He also states regular chewing of *anar* and *aloo bukhara* is useful. Experimental and clinical trials related to the safe use of *anar* (Kusumawati *et al.*, 2016), *lemon* (*Citrus limon*) (Abdolhosseini *et al.,* 2017) *aloo bokhara* (Igwe and Charlton, 2016), *gul surkh* (Shirazi *et al.,* 2016) and *shikanjabeen lemuni* (Anjum *et al.*, 2018) during pregnancy has been published for nausea and vomiting and other diseases. In classical texts, drugs such as *anar, uunab, behidana, goazaban, zanjabeel, sandal, gul surkh, ood, mastagi,* etc and compound formulations such as *jawarish ood, qurs tabasheer, jawarish mastagi, gulqand, khamira marwareed, shikanjabeen lemuni, jawarish anarain*, are in use during pregnancy for different ailments (Al-Qamari, 2008; Bashir *et al.,* 2019; Majusi, 2010). Few clinical studies are published regarding the safe use of these drugs during pregnancy for different ailments summarized in table 1 and 2. (Abdolhosseine *et al.,* 2016; Ahmed *et al.,* 2017; Kennedy *et al.,* 2016; Kusumawate *et al.,* 2016; Myhre *et al.*, 2013; Vilgoen *et al.*, 2014; Ziaei *et al.*, 2001) *Gul-e-banafsha* (*Viola odorata*), *revand chini* (*Rheum australe* D. Don), and *halela* (*Terminalia chebula* Retz.) would be useful for the prevention of infection (Rushd, 2017).

Prophylactic gargling with a decoction of *sumaq* (*Rhus coriaria* L.), *rub-e-toot* (*Morus nigra* L.), *rub-e-jauz* (*Juglans regia* L.) and *arqe-gulab* before sleep may be advised (Razi, 1991). Most of the Unani scholars mentioned that *majun* (2.5g) of *sibr* (7g), *zafran* (3.5g) and *murr* (3.5g) daily or twice a week is specifically very useful during any epidemics or *huma-i-wabaiya.* (Khan, 1983; Khan, 2011; Rushd, 2017; Razi, 2008; Samarqandi, 2009; Sina, 2009; Sina, 2010).

During pregnancy, the use of this formulation is uncertain as *sibr* has emmenagogue and abortifacient properties, though topical application in pregnancy is safe (Ahmed *et al.,* 2017). Tablet of *kafoor* (10g), *dooranja qrabi* (10g), *jadawar* (6g) mixed with *gul surkh* (as required), 3 tablets of 500mg per day in the normal individual would be useful for the prevention of epidemics (Khan, 1983). As per Unani guidelines (2020) of the Ministry of AYUSH, *tiryaq-e-arba* (3-5g) could be used as prophylaxis during COVID-19 as it has *dafa-i-sumoom* (antidote) property. However, Unani pharmacopoeia has indicated its use during pregnancy for the expulsion of a dead fetus and to ease labour because of its labour inducing and emmenagogue properties (Government Unani Pharmacopoeia, 1988). Almost all Unani scholars have advised that *tiryaq-e-wabaiya* and *tiryaq-e- afi* are useful in any epidemics. In the medieval period, *tiryaq-e-nazla* was advised for respiratory catarrhal inflammations and influenza (Khan, 1981).

In this perspective, direct reference for use of these medicines in COVID-19 and pregnancy is not available, which needs further evaluation and

research. Unani physicians gave much emphasis to *tabbaiyat mudabir badan* and were aware of the immune-boosting effect of citrus fruit. Most of these Unani drugs such as *anar, imli, halela, banafsha, zafran, amaltas pulp, turanjabeen, vinegar, toot* and *arq-e-gulab* have been proven for antimicrobial, anti-inflammatory, immunomodulatory and antioxidant properties. They are used for health promotion (Nikhat and Fazil. 2020) and found safe during pregnancy (Table 2). Likewise, *khamirajat* has cardiotonic property.

Immune enhancers: To boost the immunity *khamira goazaban* 10 g with *warqa nuqra* 1 number or *khamira goazaban joharwala* 5 g along with other drugs potentially would be useful in COVID-19 (Khan, 1983). *Khamira marwareed* and *asgandh* are advocated as immunity enhancers in Unani guidelines for the practitioner on COVID-19 (2020). The Ayurvedic Rasayanas are known for their immune-modulation and rejuvenation properties, which are important in COVID-19 management. Several *in-vitro*, animal and clinical studies have demonstrated the immune-modulatory effects of the drugs such as *asgandh* (*Withania somnifera*), *gilo* (*Tinospora cordifolia*), and *amla* (*Emblica officinale*) among many others (Sarika *et al.,* 2020). The same medicines are also used in Unani medicine. Kim and Su (2020) attributed that the psycho-neuro-immunity for Covid-19 prophylaxis includes diet, sleep and immunity-boosting, which is gaining much attention. Though some compounds and extracts of herbal drugs do not show direct antiviral activity *in-vitro*, to resist viral infection, they are used to enhance or regulate immune function by promoting phagocytosis via the reticuloendothelial system, by inducing interferons and enhancing macrophage activation that stimulates the production of IL-1 (Wang *et al.,* 2006).

***Ilaj bil ghida*/Dietary modifications:** Unani physicians stated that overeating, starvation and staying thirsty are considered detrimental as they have adverse effects on the bodily constitution (Sina, 2009). During epidemics, it is advised to avoid a moist, salty and spicy diet and to eat a less and easily digestible diet (Razi, 2008). *Masoor dal* (red lentils), *urad dal* (black lentils) and bottle gourd have been mentioned as useful in plague-like epidemics (Razi, 2008). It is also advised to avoid meat, fruits with high water content and sweets. Meats of birds found in mountains are preferred over animal meat (Khan, 2011; Razi, 2008; Rushd, 2017; Aksir Azam). The restrictions to have animal meat and seafood would be perhaps to prevent the zoonotic spread of infections. Seafoods and animals living near the ground are more predictable to be infected than those living at higher altitudes and in deep sea. It is advised to consume citrus and sour fruits, especially apples, grapes, lemon, etc (Khan, 2011). Khan (1983) advised having a light and easily digestible diet such as soup, *ash jo* (barley water) with *sharbat banafsha* or *moong dal* (red lentils) with *chapatti* (Indian bread). In place of water warm *arq-e-mako* or *arq-e-goazaban* would be useful during epidemics.

Hakeem Arzani writes during epidemics frequently consuming cow *ghee* and its massage is useful. *Hilteet* (asafoetida) is mentioned as especially useful during epidemics (Khan, 2011). However, the use of asafoetida during pregnancy is uncertain as it has emmenagogue properties (Kabir al-Din, 2007). Ibn Sina suggested the use of sour diets such as *ab angoor kham*, *samaq*, *ab lemoni* and *ab anar* in *huma-i-wabaiya*. Further, pickles made in vinegar are useful to prevent epidemic infections (Khan, 2011; Sina, 2009). The aforementioned sour diets potentially can be used during pregnancy as they are safe during pregnancy (Table 2).

Clinical practice guidelines on the use of Unani medicine for respiratory symptoms and flu-like epidemics and a possible approach for treating COVID-19 infection

Theories from Unani medicine to formulate treatment are based on cause and symptom-based diagnosis. This method is increasingly stressed in other disciplines. The presently available data proposes that COVID-19 infection during pregnancy has similar clinical manifestations and illness severity to non-pregnant adults (Farida *et al.,* 2020; Lui *et al.,* 2002; Omer *et al.,* 2020). It ranges from mild to severe and fatality depends on the severity of the illness, associated co-morbid conditions and age of patients. The COVID-19 patients mainly presented with fever, dry cough, sore throat shortness of breath, fatigue, upper airway congestion, sputum production and myalgia/arthralgia (Chan *et al.,* 2020). Similar symptoms have been described in Unani texts in the chapter related to *nazla-i-wabaiya* (Khan, 1983; Khan, 2011; Samarqandi, 2009) and *huma-i-wabaiya* (Khan, 2011; Sina, 2009; Sina, 2010; Razi, 2008). Ibn Sina describes, individuals with co-morbid diseases or with weak constitution would be more susceptible to epidemic diseases and have a poor prognosis (Sina, 2009).

Symptom specific approach is as follows

- **Fever:** In *nazla-i-wabaiya,* for fever *joshanda* (decoction) of *behidana* 3g, *unnab* 5 pieces, *sapistaan* 9 pieces and *khaksi* (*Sisymbrium adenophorum*) 5 g with *sharbat banafsha* 20 g morning and evening (Khan, 1983) is advised. The national advisory for Unani medicine published by the Ministry of AYUSH for COVID-19 also advocated the use of the aforementioned medicine for prophylaxis and to treat mild cases. In *huma-i-wabaiya*,

qurs kafoor with buttermilk or *arq-e-gulab* orally and vinegar mixed water would be advisable to reduce fever (Sina, 2009). Further, in *huma-i-wabaiya*, to relieve fever, *istifragh* of the morbid matter is initially recommended by *fasd* (venesection) in *ghalaba dam* and *mushil* (purgation) in *ghalaba* of other *khilt* (humours) (Sina, 2009). According to Unani physicians, *fasd* and *mushil* are not advisable during the first and last trimester of pregnancy (Razi, 2001). To reduce fever, *qur tabasheer kafoori* (3g) and *rab anar tursh* (10g) orally are also advocated (Khan, 2011). The other compound formulations useful in fever are enlisted in Table 1. Khan (2011) advocated the use of *dawa mushk barid mufarid, tariyaq al zayb, jawarish marjan*, and *majun rahat*. The Unani drugs present in the aforementioned *joshanda* and *sharbat* could be used in pregnancy as safety data is available. Jabin and Aman (2010) discussed that *banafsha* is safe in pregnancy and children (Jabin *et al.*, 2010). The flower *V. odorata* contains active compounds eugenol that has antioxidant, antipyretic, and antiviral activities (Jasim *et al.*, 2018). Hong *et al.* (2015) proved anti-influenza activity of betulinic acid from *Zizyphus jujuba* on influenza A/PR/8 Virus. Phenolic contents of *behidana* consisting of polymeric procyanidins that showed strong anti-influenza viral activity on the hemagglutination inhibition test (Sajid *et al.*, 2015; Wang *et al.*, 2006) and antioxidant activities (Hamauzu *et al.*, 2005). *Sapistan* has immunomodulatory, antimicrobial, anti-inflammatory, antipyretic, analgesic and antioxidant properties (Al Snafi, 2016; Gupta and Kaur, 2015). *Khaski* has antipyretic activity (Al-Jaber, 2011) and it is used during pregnancy (Saber *et al.*, 2019; Kordi *et al.*, 2014). Herbal medicines play an essential role in traditional medicine in India, Japan, China, Korea, and Colombia (rural areas), where they are frequently the therapeutic choice to cure influenza and concomitant infections. Herbal drugs act as anti-influenza agent works directly by restraining the virus or indirectly by inducing interferon or regulating immune functions (Wang *et al.*, 2006).

- **Cough and sore throat:** In severe cough in place of *sharbat banafsha*, *sharbat kashkash* 20 g or *sharbat ejaz* 20 g or *khamira kashkash* 7g oral along with aforementioned *joshanda* would be advised. To relieve sore throat, *sharbat toot* 20 g in place of *sharbat banafsha* would be added. *Laooq khayar shamber* (10g), and *laooq motadil* (10g) boiled in *arq-e-goazaban* (12g) could be advised to relieve cough (Khan, 1983). The guidelines of Unani advisory for COVID-19 (2020) to relieve congestion of throat and cough, inhalation of *arq-e-ajeeb* (2-5 drops), 3 to 4 times a day is encouraged. The other symptom-specific compound formulations useful in cough are *habb-e-surfa, khamira-e-banafsha, laooq-e-sapistan, sharbat-e-sadr*, etc (Table 1).
- **Difficulty in breathing:** The compound formulations that could be used in difficulty in breathing are *laooq-e-katan, habb-e-hindi zeeqi, joshanda zeequn nafas*, etc (Table 1).
- **Chest pain in pleurisy or pneumonia:** In case of chest pain or pneumonia associated with cough warm paste of *qurooti* (ointment) *aarad karsana* (Table 1.) 10 g mixed with powder of *zafran* (1g) and *sibr* (*Aloe vera* L. sap) (1g) would be applied on the chest wall at the pain site and covered with a cotton bandage (Khan, 1983; Samarqandi, 2009) to relieve pain. In respiratory discomfort, the application of *roghan-e-baboona sada* on the chest is advocated as per National guidelines for Unani practitioner for COVID-19 (2020).
- **Diarrhoea and thirst:** In case of associated diarrhoea, *habb-ul aas* (*Myrtus communis* L.) and *tabasheer* (*Bambusa bambos* L.) are also prescribed. *Sheera tukhm-e- kahu* (*Lactuca sativa* L. seed) may be given to relieve thirst (Rushd, 2017). Scientific studies suggested that *Myrtus communis* has anti-inflammatory, and antiviral (Masoudi *et al.*, 2016) activities (Table 2). Essential oils of *M. communis* showed anti-malarial activity. Flavonoids and anthocyanins in berries extract of *M. communis* showed antioxidant properties (Sumbul *et al.*, 2011).

  Various other drugs have also been mentioned in pharmacopoeia to treat flu-like illnesses, epidemics fever and respiratory symptoms. The formulations, their rational use, antimicrobial and antiviral activities are summarized in Table 1. Published data related to *in-vivo* and *in-vitro studies* show that these drugs have anti-tussive, anti-inflammatory, immunomodulatory, antimicrobial, antioxidant and antipyretic activities (Nikhat and Fazil, 2020).

  Alamgeer *et al.*, (2018) had reviewed a total of 384 plant species used in traditional medicine for respiratory disorders in Pakistan for ethnomedicinal and pharmacological evidence. They found that published data on pharmacological studies for 53 plants used in respiratory disorders is available. Some of the medicinal plants pharmacologically proven were *lahsun, behidana, licorice, kalonji, tulsi, banafsha, zanjabeel, unnab*, etc for flu-like illnesses, antihistamine, anti-allergic, a bronchodilator, antitussive and antiasthmatic effects.

Safety of single drugs and compound formulations during pregnancy: Though direct safety evidence of aforementioned medicines advised to be used in COVID-19 infection is not available few clinical trials are available regarding the safe use of some single drugs and compounds formulations during pregnancy for other ailments. For example, single drugs such as *zanjabeel, lahsun, sibr* (topical), *pudina, baboona, unnab*, (Ahmad *et al.*, 2017), *behidana*, (Shakeri *et al.*, 2018), *anar* (Abdol Hosseini *et al.*, 2016), *pudina, methi, lemon* (John and Shantakumari, 2015) are safe as per published scientific

studies (Ahmad *et al.,* 2017; John and Shantakumari, 2015). Compound formulations such as *khamira marwareed* (Mustafaa *et al.,* 2001) *katan, shikanjabeen lemoni*, etc are safe as per published scientific studies. *Katan (*flaxseed) is useful in cough, and found safe during pregnancy. One of the studies investigated the role of polyunsaturated fatty acids (PUFAs) consumption during pregnancy and its influence on allergy and respiratory diseases. They concluded that PUFAs act via several mechanisms to modulate immune function (Shek *et al.,* 2012). However, clinical trials are needed to prove the effectiveness of drugs and their effects on the fetus to establish a standardized treatment for pregnant women with COVID-19 (Luo and Yin, 2020). Many compound formulations are given during pregnancy however, we found very few documented studies conducted during pregnancy such as *khamira marwareed* and *shikanjabeen lemoni.*

Antiviral drugs: Guidelines for Unani practitioner for COVID-19, Ministry of AYUSH (2020) have mentioned *kalonji* (*Nigella sativa*), garlic (*Allium sativum*), *zanjabeel*, *aslassus* (*Glycyrrhiza glabra*), the pulp of *khayar shamber* (*Cassia fistula*), *afsanteen* (*Artemisia absinthium*), *tukhm-e-kasoos* (*Cuscuta reflexa* seed), *gilo* (*Tinospora cordifolia*) have antiviral property. Further, *amla* (*Emblica officianlis* L), *murr* (*Commiphora myrrha* Ness) *khaski* (*Sisymbrum oorio* L.), *ood saleb* (*Poennia officinalis),* and *kaakrasangi* (*Rhus succedanea*) (Khare, 2007) have been proven for the antiviral property. However, the effect of the above-mentioned drugs against COVID-19 is not being claimed. Allin presence in garlic has antiviral activity (Sharma, 2019). The drugs safe during pregnancy are enlisted in Table 2. Particularly, single Unani drugs and compound formulations (summarized in Table 1and 2) that show superior maternal and fetal safety would be probably recommended for pregnant women with COVID-19 to curtail fever duration, relieve symptoms, prevent disease progression and reduce mortality.

Eventually, Unani medicine should be evaluated with designed clinical trials, either used alone or integrated with conventional medicine, to prove the effectiveness of drugs and recovery of patients suffering from novel coronavirus infections. Further, clinical trials are also needed for the hour to prove the effects on the fetus to establish a standardized treatment for pregnant women with COVID-19. More evidence of the safety of traditional Unani medicine and other traditional system is also warranted (Luo and Yin, 2020).

Natural compounds with inhibitors of Covid-19 infection: It has been reported that the patients with SARS-CoV infection have been detriment from Traditional Chinese Medicine treatment, including lessening of side effects of conventional therapeutics (Yang *et al.,* 2020). Aanouz *et al.,* (2020) have evaluated Moroccan medicinal plants as inhibitors of COVID-19 with computational investigations. The results of molecular docking showed that Crocin, Digitoxigenin, and β-Eudesmol molecules from 67 molecules of natural origin have potential as inhibitors against the coronavirus on the *in-vitro* study. Potential natural compounds such as scutellarin, hesperetin, baicalin, nicotianamine, and glycyrrhizin by molecular docking were found that these molecules could interact with ACE2 and inhibit it and thereby prevent the infection of SARS-CoV-2 (Yang *et al.,* 2020).

Scientific studies in other Traditional Medicines in COVID-19 infections: The recommended Chinese Medicine formulations during the medical observation period involved are *huo-xiang-zheng-qi* capsule (for patients presented with fatigue and gastrointestinal disorder) and *jin-hua-qing-gan* granules, *lian-hua-qing-wen* capsule *or shufeng-jie-du* capsule (for patients presented with fatigue and fever) etc. The treatment period is followed by a rehabilitation stage (lung and spleen *qi* deficiency or *qi* and *yin* deficiency) (Chan *et al.,* 2020).

Ang *et al.,* (2020) in systematic research has summarized a total of 28 traditional medicine guidelines that provide treatment measures for COVID-19. In one study, complementary and Chinese medicine as integrative medicine was given to prevent and control postpartum infection. The patient was given an intravenous injection of azithromycin, oral *Lianhua qingwen* capsules (Chinese medicine), and oseltamivir antiviral drugs along with intermittent oxygen inhalation (Khan *et al.,* 2020). Ziai and Heidari examined the 20 plant extracts and observed the largest inhibitory effect on ACE exhibited by *Cerasus avium* (L.) Moench, *Alceadigitata* (Boiss.) Alef, and *Rubiatinctorum* L, showed up to 100% effect and *Allium sativum* L., *Citrus aurantium* L., *Peganum harmala* L. and *Berberis integerrima* showed an inhibitory effect of up to 70% or more. Thus, these herbal products could be considered for the treatment of the COVID-19 outbreak subsequently after the necessary in-vitro and in-vivo evaluation (Heidary *et al.,* 2020). One study concluded that Chinese herbal treatments classically used for treating viral respiratory infection might contain direct anti-2019-nCoV natural compounds. They found that 26 herbal plants were related to regulating viral infection, immune/inflammation reactions and hypoxia response (Zhang *et al.,* 2020).

- ***Lianhuaqingwen* Capsule:** The researchers found *Lianhuaqingwen* capsule (LH-C) is a traditional Chinese medicine (TCM) formula that inhibited the proliferation of influenza viruses of various strains in vitro, with the 50% inhibitory concentration (IC50) ranging from 0.35 to 2 mg/mL. It also suppressed the virus "*induced NF-kB activation and alleviated virus-induced gene expression of IL-6, IL-8, TNF-a, IP-10, and MCP-1 in a dose-dependent manner*". It exerted broad-spectrum effects on a series of influenza viruses, including the newly emerged H7N9, and particularly regulates the immune response of virus infection (Ding *et al.,* 2017).
- **Glycyrrhizin uses in pregnancy:** A study showed that up to 60% of pregnant women use herbal-based alternative medicines. Licorice is one of the most

frequently used drugs in China. Glycyrrhizin is considered to be the main bioactive ingredient in licorice, which is then metabolized to glycyrrhetinic acid. It shows antiviral, anti-inflammatory, antiallergic, and immune regulating effects in various studies. "*Glycyrrhiza had anti-SARS-CoV activity utilizing neutralization and plaque determination and it also impairs virus adsorption and membrane penetration in the early stage of virus replication, which is expected to make it a specific drug for the treatment of COVID-19.*" The maternal and fetal safety of glycyrrhizin is a major concern in pregnant women with COVID-19. In human experiments, Choi *et al.*, in a prospective study on pregnancy outcomes of 185 singleton pregnancies concluded that there was no difference between the main malformations in glycrrhiza and the control group. 91% of the exposed women used a higher dose of licorice, without an increased risk of preterm labour (< 37 weeks). Therefore, they believe that licorice is not a major teratogen or a risk factor for preterm birth. Therefore, glycyrrhizin was proposed as an antiviral drug, while dosage, form, and measurement should be considered in the clinic (Zhao *et al.*, 2020). There are many ongoing Traditional Chinese Medicine clinical trials for the treatment of SARS-CoV-2 infection (Yang *et al.*, 2020).

CRITICAL INTERPRETATION AND CONCLUSION

To conclude, it is a critical moment to overcome the current Covid-19 pandemic infection caused by the novel coronavirus, SARS-CoV-2. Further, understanding the effect of this infection especially on pregnant women and neonates is still deficient. It is expected these epidemics and pandemics will continue to occur and would be more aggressive than ever with the emergence of new organisms. In this context, COVID-19 pandemic infection provided a chance to test the true value of traditional systems of medicine in treating emerging contagious diseases because of the scarcity of strong evidence-based regimens. Furthermore, we have to strengthen the research to provide evidence-based studies for the medical management of pregnant patients with COVID-19 infection. Some regimens are recommended for pregnant women with COVID-19 in traditional Chinese Medicine although data on its effectiveness and safety need further evaluation. Therefore, the need of the hour is to develop new effectual methods of infection control that are reachable to the mass. The Unani treatments described in this manuscript are effective, cost-effective, and some of the single and compound drugs are safe during pregnancy for prevention and treating mild symptomatic cases of flu-like illnesses.

Hence, the goal of this manuscript was to analyze the overview of COVID-19 infection during pregnancy in contemporary medicine, concept and practices in Unani medicine for epidemic diseases in general and pregnancy constructed principally on observation and clinical experience. Additional safety of Unani drugs for the prevention and treatment of mild symptomatic cases of Covid-19 and pregnancy was also reviewed. Justifiably, in Unani medicine, a common term '*waba*' is used and does not mention epidemics and pandemics as separate entities. Interestingly, the concepts described in Unani classical texts primarily focused on air-borne respiratory infections among all epidemics and the role of climate or weather change has also been implicated in the spread of infectious and epidemic diseases. This need to be further validated by scientific studies that biodiversity has a role in epidemics. The concepts and practices of preventive measures such as quarantine, isolation, control of the environment, social distancing, hygiene, diet and immune-modulation explained in Unani medicine continued to be the basic canon for infection control that remain the same in contemporary preventive medicine too. Several bioactive compounds of herbal medicines such as phenols, flavonoids, eugenol, etc have significant pharmacological (anti-inflammatory, antipyretic, antioxidant, immunomodulatory, antimicrobial and antiviral) activities.

Further, we listed the use of the single Unani drugs and compound formulations that are safe during pregnancy such as vinegar, *gulab, lahsun, anar, zanjabeel*, etc. Published data on pharmacological studies for 53 plants used in respiratory disorders is accessible. Some of the medicinal plants are pharmacologically proven for flu-like illnesses such as *lahsun, uunab, behidana, aslassus, banafsha, zanjabeel, unable*, etc. They have anti-influenza, antihistamine, anti-allergic, bronchodilator, antitussive and anti-asthmatic effects. These above-mentioned drugs are safe during pregnancy and can benefit to reduce the disease burden. The studies may carefully be conducted to identify novel anti-human coronavirus natural compounds that may eventually prove to be effective and safe during pregnancy for the treatment of SARS-CoV-2 as an adjunctive therapeutic option for health promotion and disease prevention and management. The experimental studies are recommended to elucidate the mechanism underlying the therapeutic effect of Unani medicine in the treatment of COVID-19. Further, randomized, double-blind and placebo-controlled studies are the best way to provide the most reliable evidence for the effectiveness and safety of Unani and other traditional medicines.

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CONFLICT OF INTEREST-

The authors declare that there is no conflict of interest.

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