

Drug Shortages in Southwestern China: A Regional Data-Based Cross-Sectional Analysis

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Bo *et al.*: To Depict Drug Shortages in Southwestern China

Drug shortages have posed clinical and economic challenges to healthcare systems globally. Multiple data-based evidence on drug shortages in China is limited. This study aimed to depict drug shortage and cause of shortage in Southwest China and it was a cross-sectional study. Data was extracted from the multi-source drug shortage reporting system of Sichuan Province from 1st January, 2018 to 30th May 2021. The policy characteristics, dosage forms, shortage frequency, anatomical therapeutic chemical classification and cause for the drug shortage was analysed. There were 2184 reported drug shortages involving 870 drugs. Among the drugs, 631 (72.53 %) were chemical drugs. Injections had the highest average shortage frequency of 4.35, while 59.54 % (518/870) of the drugs in shortage was oral. All anatomical therapeutic chemical classification of drugs had been reported in shortage. The number of drugs for alimentary tract and metabolism was up to 117. As for policy characteristics, 44.48 % (387/870) and 79.54 % (692/870) fell into the national essential medicines list and national medical insurance drug list respectively. The incidence of drug shortage on the emergency drug list and national essential medicines list was significantly higher than that of the paediatric generic drug list and national medical insurance drug list ($p < 0.05$). Manufacturing problems was the main causes of drug shortage (46.10 %, 891/1998). A plethora of drugs experienced a shortage in Southwest China, encompassing nearly the entirety of the anatomical therapeutic chemical classification system. Drug shortage affected the entire drug supply chain, including production, delivery and utilization. To address this issue, it was imperative to foster enhanced collaboration among all stakeholders to mitigate and resolve the drug shortage problem.

Key words: Dosage form, epidemiology, ketamine, cardiovascular system, gynaecology, urokinase

Drug shortages have become a growing global concern, posing economic and clinical challenges to healthcare systems in high, middle and low-income countries^[1-3]. For patients, drug shortage is an impediment to the availability of appropriate therapeutic drugs, leading to increasing health care expenditure and unsatisfactory treatment outcome^[4-6]. In certain extreme cases, drug shortages can even pose a threat to patient's life^[7,8]. For medical personnel, drug shortages may require extra time and increase medication errors due to changes in treatment strategy^[9-11]. In a survey conducted by European Association of Hospital Pharmacists (EAHP) from 2019 to 2020, 95 % of hospital pharmacists, 71 % of physicians, 62 % of nurses and 89 % of other

healthcare professionals considered medicine shortages as a significant obstacle to providing optimal medical care to patients^[12]. For both the healthcare system and society, the occurrence of drug shortages would lead to an overall increase in healthcare expenditure^[13,14].

China has made considerable progress in the development of its drug supply system over the past few decades. In 2017, the National Health

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and Family Planning Commission of the People's Republic of China (now renamed as the National Health Commission of the People's Republic of China) and other eight ministries jointly issued the implementation opinions on reforming and improving the supply security mechanism of drugs in shortage, which clearly taken hierarchical coping, classified management, consultation and linkage mechanism, secured supply as the principle for solving the drug shortage problem^[15]. In 2019, the General Office of the State Council of the People's Republic of China issued the further work to improve the supply and price stabilization of drugs in shortage. In this official government document, relevant policies about drug procurement, rational use, stockpiling system and price regulation were further optimized^[16]. Till date, China has not experienced widespread or long-lasting drug shortages. The variety and quantity of drugs in China have generally been sufficient to meet clinical demand. Nevertheless, in recent years, localized or temporary drug shortages have continued to occur^[17].

A quantitative description of the frequency, duration, intensity and other characteristics of drug shortage can not only provide a comprehensive understanding of the current situation of drug shortages, but also be the first and critical step to deal with the problem^[13]. In order to achieve the aforementioned objectives, it was deemed that national or regional drug shortage surveillance data represented the optimal source for conducting such studies. However, such data-based studies on the current situation of drug shortages were very limited in China. Therefore, the objective of this study was to assess the characteristics of drug shortages based on data from the multi-source drug shortage reporting system in Sichuan Province from January 2018 to May 2021. We analysed the shortage frequency, dosage forms, Anatomical Therapeutic Chemical (ATC) classification, policy characteristics and causes of shortage to provide a descriptive overview of drug shortage in Southwest China. Furthermore, the study explored potential mitigation strategies and solutions to drug shortages.

MATERIALS AND METHODS

Research site and data source:

This was a cross-sectional study and it was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist^[18]. This study took Sichuan Province as

research site, which is located in the Southwest of China. We extracted the data from the multi-source drug shortage reporting system of Sichuan province from 1st January, 2018 to 30th May, 2021. The system consisted of four data reporting sources including; the sentinel hospital monitoring network for drug shortages in Sichuan Province, which included 126 hospitals covering tertiary hospitals, secondary hospitals and primary medical institutions. The members of the Sichuan drug shortage consultation linkage mechanism, including the Health Commission of Sichuan Provincial, the Sichuan Provincial Economic and Information Department, the Sichuan Provincial Department of Commerce, The Administration for Market Regulation of Sichuan Provincial, The Sichuan Provincial Healthcare Security Administration, The Sichuan Provincial Administration of Traditional Chinese Medicine, The Sichuan Medical Products Administration and the Municipal (State) Health Commission of Sichuan Province and Pharmaceutical Manufacturers.

Generic name, dosage form, cause of shortage, and reporting source were directly extracted from each reported drug shortage. In addition, another six characteristics were considered of the reported drugs in shortage; the ATC classification maintained by World Health Organisation (WHO). The 2018 edition of the National Essential Medicines List (NEML)^[19]. The 2021 edition of the National Medical Insurance Drug List (NMIDL)^[20]. The list of demonstration drugs of directly online purchased emergency (rescue) drugs (chemicals and biological products) released in 2015 (hereinafter referred as the Emergency Drug List (EDL))^[21]. The list of demonstration drugs of directly online purchased paediatric generic drugs (chemicals and biological products) released in 2015 (hereinafter referred as the Paediatric Drug List (PDL))^[21]. The list of demonstration drugs of directly online purchased obstetrical and gynaecological generic drugs (chemicals and biological products) released in 2015 (hereinafter referred as the Obstetrical and Gynaecological Drug List (OGDL))^[21]. In the meantime, drugs were classified as chemical drugs, Chinese traditional medicines, biological products, health care products according to the initial letter of drug approval number issued by the national medical products administration^[22]. To ensure data quality, the generic names were verified individually through searching the official online drug inquiry platform of the national medical products administration^[22].

Statistical analysis:

The number of reported shortage and drugs was counted for different drug type, dosage form and ATC classification. The Average Shortage Frequency (ASF) was then calculated using the following formula:

ASF=The number of reported shortages/the number of drugs

Comparing all the reported drugs in shortage with the NEML, NMIDL, EDL, PDL and OGD, the proportions of drugs in shortage in each list was calculated. The Chi-square test was used to test whether there was difference in the proportions. The $p \leq 0.05$ was considered significant and was adjusted by Bonferroni when comparing pairwise. Data input and cleaning was completed using Microsoft Excel 2016. IBM Statistical Package for the Social Sciences (SPSS) for Windows 20 was used for statistical analysis.

RESULTS AND DISCUSSION

From 1st January, 2018 to 30th May, 2021, a total of 2184

drug shortages were reported. Among the multiple data source, tertiary sentinel hospitals reported the most drug shortage (651, 29.69 %) (Table 1). In total, 870 drugs were identified as being affected by the reported shortages. The ASF was 2.51 (2184/870). In terms of each drug, the shortage frequency for urokinase was upto 91, followed by ketamine (52), benzathine benzylpenicillin (47), nitroglycerin (46) and posterior pituitary (40) (fig. 1).

Among all the drugs, chemical drugs and Chinese traditional medicines accounted for 97.24 % in total, with 72.52 % (631/870) for chemical drugs and 24.71 (215/870) for Chinese traditional medicines. Biological products and health care products only accounted for 2.41 % and 0.34 % respectively. The ASF of chemical drugs was 2.95, which was much higher than other drug types. As for dosage forms, 59.54 % (518/870) of the drugs in shortage was oral dosage, followed by injectable (27.82 %, 242/870), other (6.21 %, 56/870) and external dosage (6.21 %, 54/870). Notably, the ASF of injectable dosage was upto 4.35, higher than any other dosage forms (Table 2).

TABLE 1: DATA SOURCES OF DRUG SHORTAGE IN SICHUAN PROVINCE FROM 1st JANUARY, 2018 TO 30th MAY, 2021 (n, %)

| Data source | Reported drug shortages (n=2184) |
|---|----------------------------------|
| The sentinel hospital of drug shortage monitoring | |
| Tertiary hospitals | 644 (29.49) |
| Secondary hospitals | 301 (13.78) |
| Primary medical institutions | 319 (14.61) |
| Members of Sichuan drug shortage linkage mechanism | |
| The Sichuan provincial healthcare security administration | 421 (19.28) |
| The Sichuan medical products administration | 61 (2.79) |
| The Sichuan provincial department of commerce | 31 (1.42) |
| The municipal (state) health commission | 314 (14.38) |
| Pharmaceutical manufacturers | 93 (4.26) |

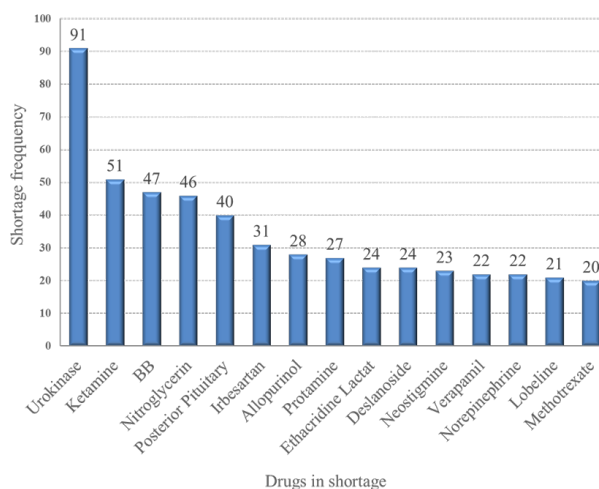


Fig. 1: The top 15 drugs of frequencies of shortage in Sichuan Province during 1st January, 2018 to 30th May, 2021

TABLE 2: TYPE AND DOSAGE FORM OF DRUGS IN SHORTAGE IN SICHUAN PROVINCE FROM 1st JANUARY, 2018 TO 30th MAY, 2021

| Characteristics | Reported drug shortages (n, %) (n=2184) | Number of drugs (n, %) (n=870) | ASF |
|-------------------------------|--|-----------------------------------|------|
| Type | | | |
| Chemical drugs | 1861 (85.21) | 631 (72.53) | 2.95 |
| Chinese traditional medicines | 279 (12.77) | 215 (24.71) | 1.3 |
| Biological products | 40 (1.83) | 21 (2.41) | 1.9 |
| Health care products | 4 (0.18) | 3 (0.34) | 1.33 |
| Dosage form | | | |
| Injectable | 1,053 (48.21) | 242 (27.82) | 4.35 |
| Oral | 959 (43.91) | 518 (59.54) | 1.85 |
| External | 86 (3.94) | 54 (6.21) | 1.59 |
| Other | 86 (3.94) | 56 (6.44) | 1.54 |

In accordance with the ATC classification maintained by WHO, 631 chemical drugs and 21 biological products in shortage were classified into all the 14 categories. The number of drugs for alimentary tract and metabolism was upto 117, accounting for 17.94 % (117/652). The ASF for each drug belonging to cardiovascular system, blood and blood forming organs, systemic hormonal preparations, excl. Sex hormones and insulin was >4. The top 3 drugs in shortage in each category were shown in Table 3.

Among the 870 drugs, (44.48 %) and 79.54 % (692/870) of the drugs fell into the NEML and NMIDL respectively. The incidence of drug shortage on NEML was significantly higher than that of NMIDL ($p < 0.05$). In addition, 72.88 % (43/59) of the drugs on EDL experienced shortage, which was significantly higher than that of PDL (33.93 %, $p < 0.05$) (Table 4).

Among the reported drug shortages, 441 did not report the cause of shortage, and 242 reported multiple causes. Ultimately, 1998 causes of shortage were identified. The causes of shortage could be identified into 4 principal categories; manufacturing problems, distribution problems, discontinuation and other. The most reported cause was manufacturing problems (46.10 %, 891/1998), and the specific reason for insufficient production capacity included production line renovation (17.17 %, 343/1998), shortage (16.52 %, 330/1998) and monopoly (10.51 %, 210/1998) of raw material, and large demand led by the volume-based procurement (0.40 %, 8/1998). The 2nd most common reported cause was distribution problem (23.17 %, 463/1998), including pharmaceutical supplier's reluctance to supply drugs because of small drug demand (9.61 %, 192/1998), remote region (8.31 %, 166/1998) and low

transaction price (4.55 %, 91/1998). Discontinuation accounted 8.71 % (174/1998) of the reported cause of shortage. In addition, rising drug price and failure of bid played an important role in drug shortages, with 13.21 % (264/1998) and 7.66 % (153/1998) respectively (fig. 2).

There were 2184 shortages reported by different data source from January 2018 to 30th May, 2021 in Sichuan Province, which included 870 drugs with the ASF of 2.51 per drug. Compared with other provinces, the ASF of Sichuan Province was low. Ma *et al.*^[23] found the ASF of Hubei province was 3.81 (2439/640), and in another literature, the ASF of Liaoning was up to 3.83 (964/252)^[24].

In this study, drug shortages occurred at all levels of hospitals in Sichuan Province. Especially, it was more serious in tertiary hospitals than in other levels of hospitals. This may be caused by the great demand for drugs in tertiary hospitals^[25]. Patients in China always tend to go to higher level of medical institutions regardless of the severity of disease^[26]. From the whole drug supply chain, manufacturers should be the first to know an impending drug shortage, then the supplier, and finally the demand-side like hospitals. In other words, manufacturers should be more active and take more responsibility for reporting drug shortages to reserve sufficient time to develop contingency plans for related stakeholders. However, in our study, reported shortages from sentinel hospitals was far more than other reporting sources, just 4.26 % (93/2184) from pharmaceutical manufacturers. This definitely leads to poor timeliness of drug shortage information and make it more difficult to restore the supply after the market disruptions^[27]. In China, some measures have

been developed to improve the timeliness of drug shortage, including the measures for supervision and administration of drug production issued in 2020 which requires the holder of a pharmaceutical manufacturing license to report the unplanned drug halted production in 3 d^[28], and the multi-source information collection platform for drug shortages launched in November

2021 to collect information of drug shortage from different stakeholders. But according to this study, the measures described above might not had the desired effect. Therefore, we proposed the establishment of a stricter monitoring mechanism for drug shortages and appropriate disclosure of information on drug shortages.

TABLE 3: ATC CLASSIFICATION OF DRUGS IN SHORTAGE, IN SICHUAN PROVINCE FROM 1st JANUARY 2018 TO 30th MAY 2021

| ATC code | Reported drug shortages (n, %) | Number of drugs (n, %) | ASF | Top 3 drugs in shortage |
|----------|--------------------------------|------------------------|------|--|
| C | 338 (17.78) | 68 (10.43) | 4.97 | Nitroglycerin, Irbesartan, Deslanoside |
| B | 281 (14.78) | 60 (9.20) | 4.68 | Urokinase, Ethacridine Lactate, Arginine Hydrochloride |
| N | 227 (11.94) | 67 (10.28) | 3.39 | Ketamine, Neostigmine, Diazepam |
| J | 219 (11.52) | 94 (14.42) | 2.33 | Benzathine Benzylpenicillin, Oseltamivir, Protionamide |
| A | 205 (10.78) | 117 (17.94) | 1.75 | Vitamin AD, FamotidineCalcium Gluconate, |
| R | 139 (7.31) | 54 (8.28) | 2.57 | Lobeline, Nikethamide, Budesonide |
| L | 123 (6.47) | 39 (5.98) | 3.15 | Methotrexate, Cytarabine, Celecoxib |
| V | 82 (4.31) | 23 (3.53) | 3.57 | Protamine, Pralidoxime, Naloxone |
| H | 81 (4.26) | 18 (2.76) | 4.5 | Posterior Pituitary, Oxytocin, Thiamazole |
| G | 66 (3.47) | 37 (5.67) | 1.78 | Conjugated Estrogens, Chlorquinaldol, Estriol |
| M | 59 (3.10) | 23 (3.53) | 2.57 | Allopurinol, Ibuprofen, Colchicine |
| S | 36 (1.89) | 26 (3.99) | 1.38 | Tobramycin Dexamethasone, Sodium Cromoglicate, Diclofenac Sodium |
| D | 35 (1.84) | 23 (3.53) | 1.52 | Calamine, Ketoconazole, Sulphur Ointment |
| p | 10 (0.53) | 3 (0.46) | 3.33 | Albendazole, Lindane, Pyrimethamine |

Note: The total number of reported drug shortages was 1901 and the total number of drugs was 652, (C): Cardiovascular system; (B): Blood and blood forming organs; (N): Nervous system; (J): Anti-infective for systematic use; (A): Alimentary tract and metabolism; (R): Respiratory system; (L): Antineoplastic and immunomodulating agents; (V): Various; (H): Systemic hormonal preparations, excl. sex hormones and insulin; (G): Genito urinary system and sex hormones; (M): Musculo-skeletal system; (S): Sensory organs; (D): Dermatologicals and (P): Antiparasitic products, insecticides and repellents

TABLE 4: DRUG SHORTAGES IN SICHUAN PROVINCE ON EACH LIST FROM 1st JANUARY, 2018 TO 30th MAY, 2021

| Lists | Number of drugs (n, %) (N=870) | Ratio (%) |
|--|--------------------------------|---------------------------------|
| NEML | | |
| Essential medicine | 387 (44.48) | 387/685 (56.50 %) ^b |
| Non-essential medicine | 483 (55.52) | - |
| NMIDL | | |
| Medical insurance drug | 692 (79.54) | 692/2860 (24.20 %) ^a |
| Non-medical insurance drug | 178 (20.46) | - |
| EDL | | |
| Emergency drug | 43 (4.94) | 43/59(72.88 %) ^b |
| Non-emergency drug | 827 (95.06) | - |
| PDL | | |
| Pediatric generic drug | 19 (2.18) | 19/56(33.93 %) ^a |
| Non-pediatric generic drug | 851 (97.82) | - |
| OGDL | | |
| Obstetrical and gynecological generic drug | 9 (1.03) | 9/22 (40.10 %) ^{a,b} |
| Non-obstetrical and gynecological generic drug | 861 (98.97) | - |

Note: ^{a,b}p<0.05

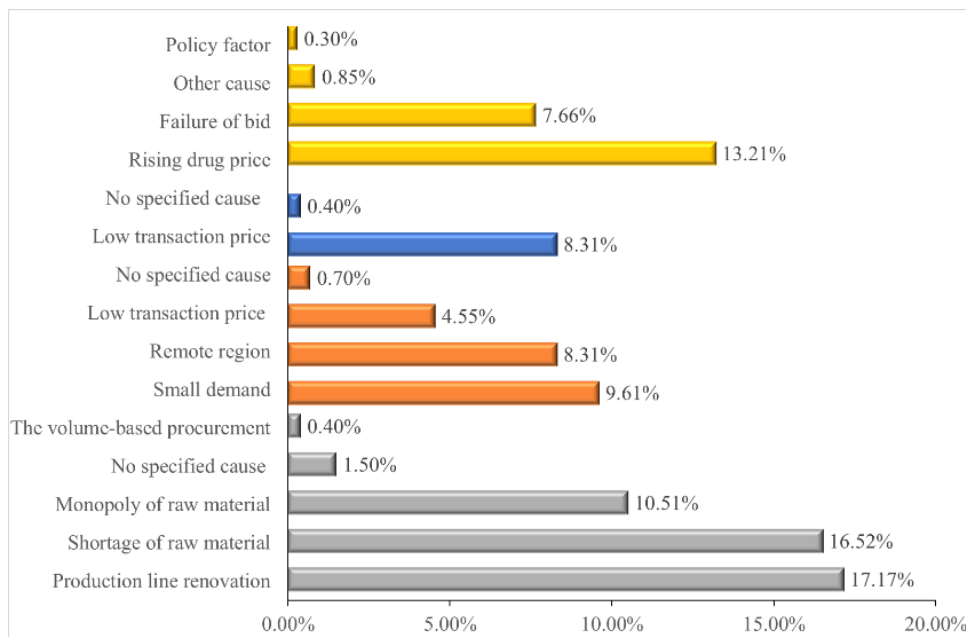


Fig. 2: Causes of drug shortage in Sichuan Province from 1st January, 2018 to 30th May, 2021

Note: A drug may be in shortage caused by multiple cause, (■): Other causes; (■): Distribution problems; (■): Manufacturing problems and (■): Discontinuation

According to previous literature, the dosage form most likely to be in short supply seemed to be inconsistent so far. In the United States of America (USA), parenteral (61.2 %) was the most drugs in shortage from 2014 to 2019^[29]. In France, injectable took upto 47.5 % of the total drugs in shortage from 2012 to 2018, which was higher than oral (43.3 %)^[30]. But in contrast, the proportion of oral (51 %) was higher than injectable (40 %) in Europe^[31]. In terms of the total number of drugs, our study was consistent with Europe, with the largest proportion of drugs in shortage being oral medicines. The underlying cause may be the great demand in clinical use of oral. But in terms of ASF, injectable was much higher than that of other dosage forms in this study, indicating higher shortage frequency of injectable. This may be partly explained by the strict Good Manufacturing Practice (GMP) for injectable. The manufacturing process of injectable was more complex than other dosage forms, so it is generally acknowledged that injectable was more susceptible to quality defects and production problem^[31-33]. Data from the Food and Drug Administration (FDA) showed that quality-related or manufacture-related shortages of injectable had been upto 75 %^[34].

As for therapeutic properties, nearly all ATC classification of drugs had been reported in shortage, but the severity of drug shortage in different ATC classifications was inconsistent. Studies in other countries or regions have showed similar results, although the specific ATC classification rank may not be the same^[1,29,35-37]. According to this study,

the cardiovascular system was the most serious classification in drug shortage with the ASF of 4.97. Nitroglycerin, as one of the most commonly used first-line drugs for acute ischemic heart disease, once it is in shortage, thousands of patients may experience serious health consequences^[38]. According to the University of Utah Drug Information Service (UUDIS) database, the shortages of cardiovascular drugs always remained a fairly constant high level^[39]. In consideration of the increasing prevalence of cardiovascular disease, ongoing shortages of cardiovascular drugs may become a public health problem^[40,41]. Although the ASF of alimentary tract and metabolism drugs was low, the number of drugs experiencing shortage was the most. The underlying reason may be the dietary uptake of high salt in Sichuan Province^[42].

In this study, 44.48 % (387/870) of the drugs in shortage were essential medicines, accounting for upto 56.50 % of the NEML, indicating that the shortage of essential medicines in Sichuan Province was quite severe. This was consistent with previous studies in China. A qualitative study conducted in Shaanxi Province showed that most drug shortage reported in the survey was essential medicines (51/95)^[43]. Yinyin found that 51.0 % (208/408) of the drugs on the provincial drug shortage lists were essential medicines^[44]. Such a high proportion of essential medicines in shortage greatly decreased the accessibility of these drugs for the public. In addition, 779.54 % (692/870) of the reported drugs in shortage were medical insurance drugs. Under such conditions, the patients and physicians had to seek for

alternative drugs, which were generally much more expensive, increasing the economic burden of disease. Therefore, more attention should be paid to the adequate supply of these drugs.

Like other studies, this study also found a high ratio of emergency drugs in shortage. An online survey included 236 emergency physicians in China showed that drug shortages occurred every month or more frequently reported by 65.7 % of the respondents^[25]. In the USA, nearly all the 30 commonly used emergency drugs experienced a shortage from 2006 to 2019^[45]. If emergency medications were unavailable, the quality of medical care would not be guaranteed, patients could experience medication errors, treatment delays, adverse outcomes, and increased healthcare costs^[46]. Drug accessibility for vulnerable groups have been of great concern. According to the drug shortage data from January 2001 to December 2015 obtained from UUDIS, 41.37 % (779/1883) of the products on shortage were used in paediatric emergency or critical care^[47]. Raw found that 62.20 % (209/336) of medications on the 2019 WHO model list of essential medicines for children had been in shortage from 2014 to 2019^[29]. Based on previous studies, the shortage of paediatric drugs in China was quite severe^[48], which was also confirmed in this study with the drug shortage incidence of PDL of 33.93 %. In addition, the drug shortage incidence of OGD was 40.10 % (9/22) in this study, indicating that pregnant women were another vulnerable group to experience drug shortage. Nixon, hold that generic drugs used in obstetric anaesthesiology were more susceptible to drug shortage^[49]. From the bioethical and moral perspective, children and pregnant women have a special claim to social protection and consideration, more management strategies should be well established to ensure the availability of paediatric and obstetric drugs and related products.

The causes of drug shortage were multifaceted and complex, and it could only be analysed summarily in this study. As in other studies, manufacturing problems topped the list^[32]. Raw material problems have been widely considered as one of the main reasons leading to manufacturing problem^[50]. In consistent with previous studies^[27,51], this study also found that volume-based drug procurement might lead to emergence of drug shortages, the underlying reason may be a sudden increase in demand for disease-specific drugs. For other three groups of cause, the root cause behind was about economic benefit^[31,52-54]. At present, the most common and important way to get access to China's drug supply chain was to win the competitive public bidding.

Meanwhile, the bid-winning prices were not allowed to be higher than the ceiling price set by government sectors, so the marketing of the drug became less profitable and less attractive for manufacturers to win the bid, which may lead to decreasing production capacity and discontinuation due to business strategy. On the other hand, when the prices were set unattainably low without considerable margins, drug suppliers would certainly be reluctant to supply after having delivered the agreed quantity of the contract^[31,55].

Based on the results of this study and the specific situation of drug shortage in China, we propose the following recommendations to solve or mitigate the drug shortage problem, including; strengthening pharmaceutical production and quality management. A real-time and sensitive monitoring system should be established to keep track of the production and supply of raw materials to warn and prevent disruption of drug production and pharmaceutical companies should be encouraged to explore stricter internal quality management systems on basis of GMP to avoid sudden drug shortages due to quality problem. Ensuring drug distribution a modern logistics system should be constructed to improve the concentration of the pharmaceutical market and enhance the stability of drug supply. A central pharmacy could be established to centralize the procurement of drugs with low clinical demand. Optimizing drug policy the taking volume-based procurement for example, terms of responsibility for the manufacturer's inability to supply drugs should be clarified in the procurement contract. And a scientific and reasonable pricing model should be explored considering drug quality and supply sustainability to avoid drug shortage caused by low price.

The data used in this study based on multiple sources, including medical institutions at all levels, administrative departments, and pharmaceutical companies, so our result could provide a rather realistic picture of the drug shortage in Sichuan Province. But two main limitations of this study should be noted. First, the data in this study was extracted from 1st January, 2018 to 30th May, 2021, when the Coronavirus Disease-2019 (COVID-19) pandemic had a significant impact on global drug supply chains. But due to the availability of data, we could not analyse the confounding effect of COVID-19. Second, most of the results of this study were descriptive and no quantitative analysis of the clinical outcomes, economic losses and social impact of drug shortages was performed, so further research was needed to assess the impact.

In conclusion, this study has fully described and analysed the drug shortage situation in Sichuan Province based on multi-source reporting data. A plethora of drugs experienced a shortage in Sichuan Province, covering nearly all the ATC classification. A large portion of the drugs were oral, but the ASF of injectable was the highest. The incidence of drug shortage on the EDL and NEML was significantly higher than that of the PDL and NMIDL. Drug shortage affected the entire drug supply chain, including production, delivery and utilization. To address this issue, it was imperative to foster enhanced collaboration among all stakeholders to mitigate and resolve the drug shortage problem.

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Conflict of interests:

The authors declared no conflict of interests.

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