ORIGINAL ARTICLE

# Estimation of Annual Need, Production and Per Capita Consumptions of Oral Morphine in Bangladesh

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## Abstract

**Background:** Worldwide, opioid analgesics prescribed for the management of moderate to severe pain in both malignant and non-malignant patients. Use of opioids for pain management is very limited in healthcare facilities of Bangladesh. For ensuring proper management this study aims to explore opioid consumption, accessibility and availability especially in cancer pain in Bangladesh.

**Methods:** This observational study used preconstructed questionnaire to estimate annual production and use of opioids at different settings. Information was obtained from annual drug report of 2020-2021 Bangladesh's Department of Narcotics Control (DNC), Director General of Health Services of Bangladesh and three pharmaceutical companies. Availability and accessibility of morphine was explored among the tertiary care centre of Bangladesh using patient's records

**Results:** Morphine and other 5 types of opioids are available in different formulations in Bangladesh. Locally only two pharmaceutical companies producing morphine though there are 3 are licensed. In last 5 years on an average 15.34 kg (range 10.9 kg – 20.1 kg) morphine produced. There are only a few hospitals where oral morphine is readily available. But almost all of them are metropolitan Dhaka based.

**Conclusion:** The low consumption of morphine indicates the poor pain management scenario of the country. Pain and palliative care professionals in Bangladesh continue to advocate for improvements which will ensure that opioids are available, accessible and affordable for all patients in Bangladesh.

**Keywords:** Oral Morphine, Annual Need, Annual Production, Per Capita Consumption, Bangladesh.

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## Introduction

The divine sanction of Opioid tincture by the god of dreams Morpheus was one of the greatest gift to earthy human. Since the discovery of "class of opioid analgesics" by Friedrich Serturner in 1804, it has become an important pharmacological tool for alleviating pain[1] and today is included in the Model list of Essential Medicines of World Health Organization (WHO)[2]. This is also integral part for treating pain in "Palliative Care" approved by the International Association for Hospice & Palliative Care (IAHPC)[3].

Despite of repeated evidence and advocacy; accessibility and availability of opioid for pain management has been neglected in Bangladesh. Communicable diseases like Tuberculosis and Malaria as well as public health problems like sanitation and vaccination are always the focus of health policy. But today's increase in non-communicable disorders such as cancer, cardiovascular disease, diabetes, and cerebrovascular disorders are adding extra burden to healthcare facilities. According to the WHO report of 2018, the total number of cancer patients was 150,781 and the mortality rate was 108,137. By the year 2030, the probable death by cancer is predicted as 4.63%.[4] But there is very limited palliative care service and only 9% of cancer patients have opioid access for their pain management.[4]

Prescribing opioids to manage malignant and non-malignant pain is practiced globally. The World Health Organization (WHO) estimates there are 5 billion people across the globe with minimal access to pain medicines. Among them, 5.5 million are terminal cancer patients and also others enduring end-of-life suffering.[5] If we look at global medical opioid consumption, upper and middle-income countries use 68% whereas lower middle-income countries use only 7%.[6] it is important to note that there is inequity in opioid accessibility, availability, and consumption for pain management around the globe. Here, Consumption is a measure of the amounts of opioids legally used in a country for medical and scientific purposes to the health care facilities that are licensed for opioid prescribing.[7] So, national annual opioid consumption per capita serves as an indicator of the capacity to provide adequate pain relief. As pain management is a vital component of quality health care, the data on opioid consumption is an indicator of the provision of palliative care. Patients' ability to obtain morphine or other opioids for their pain relief refers to opioid accessibility. Unless to make morphine available throughout the country proper morphine access by patients who are in need is not possible.

However, there are a number of barriers preventing appropriate access to Morphine. A qualitative study, in 2010, concluded that inadequate dosing, interrupted drug supply, legal restrictions, and unavailability of immediate-release morphine are the barriers to opioid use in Bangladesh.[8] The majority of physicians are unaware of the locations where patients can obtain morphine. In 2014 a survey, conducted on 1000 physicians regarding knowledge, attitude, and prescribing practice towards opioids, summarized that 85% of physicians preferred pethidine over morphine for the management of severe pain.[9] 74% physicians and 59% 'nurses are reluctant to use opioids. This is attributed as one of the main obstacles to access of morphine and other opioids.[9]

Narcotics may be essential for the management of pain, but adversity and scarcity have made its use difficult. So, initiatives to reform drug policy, and increase awareness and knowledge relating to narcotics medical use are necessary across the countries. In this situation, this study aims to estimate the annual production and per capita consumption of Morphine in Bangladesh.

## Methods

This survey used a pre-constructed questionnaire to estimate the annual production and use of opioids in different health care settings. Information was obtained from the annual drug report of 2020-2021 from Department of Narcotics Control (DNC) and office of the Director General of Health Services of Bangladesh. Local production was evaluated from reports of three pharmaceuticals related to production and marketing of different formulations of opioids in Bangladesh. Availability and accessibility of different

formulations of morphine were explored among the tertiary care centers of Bangladesh using patient records.

## Results

Local Production and Per Unit Value:

Table 1 shows different formulations of Morphine available in Bangladesh with their retail pricing. Injectable, sustained release, immediate release and oral solutions are currently available.

**Table I:** Lists the retail prices of different preparations of morphine sulfate.

| Formulation of Morphine | Cost (USD) |
|---|---|
| Injection (15mg/1ml) | $0.46/ampoule |
| Sustained Release tablet (15mg) | $0.16/tablet |
| Immediate Release tablet (10mg) | $0.10/tablet |
| Oral solution (5mg/5ml, 100 ml bottle) | $0.91/bottle |

SR=Sustained Release, IR=Immediate Release

Figure 1 shows production of oral and injectable morphine from year 2017 to year 2021. At 2017 total production was 10.9, where at 2021 it reaches approximate double amount around 20.1.

Table 2 depicts 5 other opioids- Fentanyl, Tramadol Hydrochloride, Nalbuphine hydrochloride, Oxymorphone hydrochloride, and Pethidine hydrochloride and their formulations and cost in Bangladesh. Fentanyl transdermal patch (50cg) is most costly 14.77 USD/patch, where Tramadol Hydrochloride 50mg capsule is the cheapest one (0.09 USD).

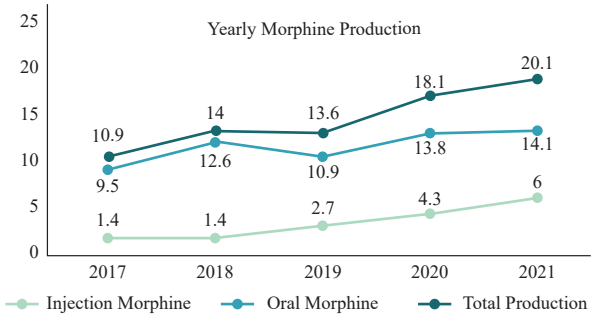


**Fig. 1:** Morphine Production from 2017 - 2021

**Table II:** Lists the retail prices of different preparations of morphine sulfate.

| Opioid | Formulation | Cost (USD) |
|---|---|---|
| Fentanyl | Buccal Tablet (100mcg) | $0.32/tablet |
| | Buccal Tablet (200mcg) | $0.58/tablet |
| | Injection (100mcg/2ml) | $0.51/ampoule |
| | Transdermal Patch (25mcg/hour) | $7.42/patch |
| | Transdermal Patch (50mcg/hour) | $14.77/patch |
| | Capsule (50mg) | $0.09/capsule |
| | SR Capsule (100mg) | $0.15/capsule |
| Tramadol hydrochloride | Injection (100mg/2ml) | $0.23/ampoule |
| | Suppository (100mg) | $0.17/suppository |
| | Per Rectal Tablet (100mg) | $0.19/tablet |
| Nalbuphine hydrochloride | Injection (10m/1ml) | $0.77/ampoule |
| | Injection (20m/2ml) | $1.28/ampoule |
| Oxymorphone hydrochloride | Tablet (10mg) | $0.26/tablet |
| | Injection (1mg/1ml) | $2.57/ampoule |
| Pethidine hydrochloride | Injection (100mg/2ml) | $0.32/ampoule |

SR=Sustained Release, IR=Immediate Release

### Yearly Oral Morphine Consumption

Figure 2 shows consumption of oral morphine was lowest at the year 2017 and reached its peak in 2019. But at 2020 the consumption rate started decreasing and reached 13 kg in 2021.

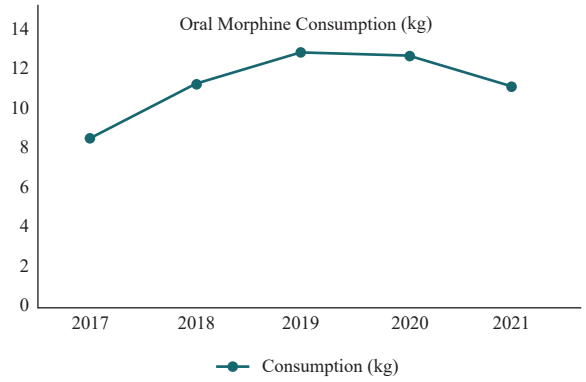


**Fig. 2:** Yearly consumption of oral morphine sulphate

**Table III:** Lists of the institutes where morphine sulfate is available.

| Name of the institute | Type of institute | Morphine IR tablet | Morphine SR tablet | Morphine oral solution | Morphine injection |
|---|---|---|---|---|---|
| Bangabandhu Sheikh Mujib Medical University (BSMMU) | University Hospital | √ | √ | √ | √ |
| National Institute of Cancer Research & Hospital (NICRH) | Public | √ | √ | √ | √ |
| Dhaka Medical College & Hospital (DMCH) | Public | Till 2018 | Till 2018 | Till 2018 | √ |
| Square Hospitals Ltd. | Private | √ | √ | √ | √ |
| Evercare Hospital Ltd. | Private | √ | √ | √ | √ |
| Ashic Oncology and Palliative Care Center | Private | √ | √ | √ | √ |
| Uttara Crescent Hospital | Private | √ | √ | √ | √ |
| Gonoshasthaya Nagar Hospital | Private | | √ | | √ |
| Delta Medical College and Hospital | Private | √ | √ | | √ |
| United Hospital Ltd. | Private | √ | √ | | √ |

SR=Sustained Release, IR=Immediate Release

### Morphine Availability & Accessibility

Table III shows the availability and accessibility of different formulations of Morphine at 10 tertiary care hospitals in Bangladesh.

## Discussion

Opioids, particularly morphine, are essential for the treatment of moderate to severe pain which is common in patients with advanced cancer. Bangladesh has an annual quota of 100 kg of morphine allocated by the International Narcotic Control Board (INCB)[10]; however, Bangladesh's Department of Narcotics Control (DNC), has allocated only 70 kg in the past years. At present, three local pharmaceutical companies have morphine manufacturing licenses. A license system, with supervision and monitoring from the DNC is in place to prevent the diversion or abuse of morphine in Bangladesh. When estimating requirements for morphine, the INCB, advises that 80% of end-stage cancer patients and 50% of HIV/AIDS patients will require morphine at an average daily dose of 67.5mg for the last 90days[10]. The current annual quota of 100 kg will be sufficient to treat only1/5 of end-stage cancer& HIV/AIDS patients who are in need of it.

The local manufacture of morphine began in 2007 when a pharmaceutical company started to prepare morphine sulphate injection followed by morphine sulphate sustained release (SR) tablets in 2009. Significant progress occurred in 2014, when a second pharmaceutical company began to produce much-needed immediate- release (IR) morphine sulfate tablets. From 2015, they also started producing morphine sulfate SR tablets and morphine oral solution. A third company also has a narcotic license and initially they had produced morphine sulfate injection which is now not available in the market. Currently, former 2 pharmaceuticals together have permission to produce 25 kg of morphine per year. But according to the Department of Narcotics Control's annual drug report for 2020-2021 and yearly production report of one of them, in the last 5 years from 2017 to 2021 an average 15.34 kg (range 10.9 kg – 20.1 kg) of morphine was produced. It is very depressing that, among 294 registered pharmaceuticals, 3 are licensed, and moreover only 2 have continued production of morphine.[11]

'Pain & Policy Studies Group of University of Wisconsin' and WHO jointly conducted a study on per capita morphine global consumption, in 2012 and summarized that the global morphine consumption was 5.99 mg/capita later which increased to 61.5 mg/capita in 2015 whereas in Bangladesh it is only 0.05mg/capita. Among the South-Asian countries, Sri Lanka's per capita morphine consumption was in the highest position with 0.38 mg/capita which improved with better metrics, 1.21 mg/capita, in 2015.[12,13]

According to the sales report and Annual Drug Report by DNC, in 2020, a total of 13 kilogram of oral morphine (immediate release, sustained release, and syrup) was consumed.[14] If we divide the total consumed milligrams of oral morphine by the number of patients who died (87263 patients) due to cancer (80% of total death) and HIV/AIDS (50% of total death) then we have observed average149.6 mg oral morphine consumed by each patient in last 90 days towards their end of life. This means daily consumption was 1.66 mg which is 40 times less than the daily consumption recommended by INCB.

Despite morphine being the most important medication, especially oral morphine, for the relief of severe chronic cancer pain, there are only a few hospitals, both Public and Private, where it is readily available. But all are metropolitan Dhaka based. 'Centre for Palliative Care' remains the main consumer of oral morphine at Bangabandhu Sheikh Mujib Medical University (BSMMU) and Square Hospitals Ltd. Department of Oncology and Radiotherapy Centre are the main prescribers. In the maximum district and sub-district governmental as well as in private hospitals of Bangladesh, injection morphine is available which is used exclusively for the management of severe cardiac or post-operative acute pain but oral morphine is not available for the management of chronic pain of cancer and HIV/AIDS patients which is more suitable and recommended.

There is one retail outlet where tablets (IR & SR) and syrup forms of morphine are available. They have 5 outlets located in Dhaka and 4 other mega cities of Bangladesh, to make oral morphine available and accessible to those patients who are seeking it. There are an additional twelve retail licensed drug stores across Bangladesh, which sell only morphine SR tablets and injections. At present, patients or their family members, many of whom live in remote areas of Bangladesh, must travel to Dhaka to obtain morphine. The majority of physicians are unaware of the locations where patients can obtain morphine.

**Conclusion**

Pain and Palliative Care providers of Bangladesh are working closely with government regulators, the department of narcotics control, and the pharmaceutical industries to improve the availability and accessibility of morphine country wide. Additionally, efforts to increase awareness among health care professionals and the general public about crucial role of morphine in the relief of pain are ongoing. There is still a long way to go before to make this essential medicine to available, accessible and affordable for all patients in need in Bangladesh.

**Limitations**

We estimate this per capita consumption depending on the total annual morphine sales report getting from pharmaceuticals and the number of patients who died by cancer & HIV/AIDS. So, this estimated per capita consumption is not based on the individual patient's consumption. Among those patients might be many patients died with severe pain without having morphine in their last days of his or her life. On the other hand, a portion of those patients might get adequate morphine according to their need.

## Declaration

**Author contributions**

Conception and development of the idea *FNB, MD, NA, AKMA*
Data collection *FNB, SAI, MS*
Data analysis *MS, MD*
Writing - Original Draft Preparation *FNB, MMK*
Review & Editing *FNB, MP, AKMA, MD*

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**Conflict of interests** None

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