

# Original Article: Complications (Pain intensity, Opioid usage, Bleeding, morbidity and mortality) following pancreaticoduodenectomy

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## ABSTRACT

**Introduction:** A comprehensive understanding of these complications, their risk factors, and appropriate management strategies is essential for surgeons and healthcare providers involved in the care of patients undergoing pancreaticoduodenectomy. Continued research, advancements in surgical techniques, and multidisciplinary collaboration are needed to further improve outcomes and reduce the incidence of complications following this challenging surgical procedure.

**Material and Methods:** This article was a retrospective observational study conducted to evaluate the incidence, clinical significance, and management of complications associated with pancreaticoduodenectomy. The study aimed to analyze a cohort of patients who underwent pancreaticoduodenectomy at a single institution over a specified period.

**Results:** Several factors were found to be associated with the occurrence of complications following pancreaticoduodenectomy. Prolonged operative time (>6 hours) was significantly associated with an increased risk of pancreatic fistula ( $p=0.043$ ) and postoperative hemorrhage ( $p=0.018$ ). Intraoperative blood loss (>500 mL) was also associated with a higher incidence of postoperative hemorrhage ( $p=0.032$ ). Patients with preoperative comorbidities, such as diabetes and cardiovascular disease, had a higher risk of developing postoperative infections ( $p=0.016$  and  $p=0.023$ , respectively).

**Conclusion:** Complications following pancreaticoduodenectomy remain a significant challenge despite advancements in surgical techniques and perioperative care. Pancreatic fistula, delayed gastric emptying, postoperative hemorrhage, and biliary complications are among the most common complications observed in this study.

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## Introduction

**P**ancreaticoduodenectomy, commonly known as the Whipple procedure, is a complex surgical procedure performed to treat a variety of diseases affecting the pancreatic head, duodenum, bile duct, and surrounding structures [1-3]. It is most frequently utilized for the treatment of pancreatic cancer, as well as other conditions such as periampullary tumors, chronic pancreatitis, and benign tumors. While pancreaticoduodenectomy offers the potential for curative treatment and improved patient outcomes, it is associated with a significant risk of complications [4-6]. This article aims to provide an overview of the complications following pancreaticoduodenectomy, their incidence, clinical significance, and approaches to management [7-9].

Pancreaticoduodenectomy is a major surgical procedure that involves the resection of the head of the pancreas, duodenum, gallbladder, common bile duct, and a portion of the stomach. Following the resection, several reconstruction techniques are employed to restore the continuity of the gastrointestinal tract, including pancreaticojejunostomy, hepaticojejunostomy, and gastrojejunostomy [10-12]. Despite advancements in surgical techniques and perioperative care, complications following pancreaticoduodenectomy remain relatively common and can significantly impact patient outcomes [13-15].

One of the most common complications following pancreaticoduodenectomy is pancreatic fistula, which refers to the leakage of pancreatic secretions from the pancreaticojejunostomy or other sites of pancreatic anastomosis. Pancreatic fistula is a significant concern due to its association with increased morbidity, mortality, and prolonged hospital stays [16-18]. The International Study Group on Pancreatic Fistula (ISGPF) has

classified pancreatic fistula into three grades based on the amount of drain output and the need for intervention, providing a standardized approach to diagnosis and management. Strategies to reduce the incidence of pancreatic fistula include meticulous surgical technique, optimal patient selection, and the use of perioperative drains and somatostatin analogues [19-21].

Another common complication following pancreaticoduodenectomy is delayed gastric emptying (DGE), which refers to the delayed resumption of normal gastrointestinal function after surgery [22-25]. DGE can lead to prolonged hospitalization, increased risk of infections, poor oral intake, and impaired patient recovery. Risk factors for DGE include preoperative malnutrition, prolonged operative time, intraoperative blood loss, and the presence of postoperative complications. Management of DGE involves supportive measures such as early ambulation [26-28], prokinetic agents, and nutritional support.

Postoperative hemorrhage is a potentially life-threatening complication following pancreaticoduodenectomy. It can manifest as intra-abdominal bleeding, gastrointestinal bleeding, or wound hematoma. Postoperative hemorrhage is associated with increased mortality and often requires surgical intervention to achieve hemostasis [29-31]. Risk factors for postoperative hemorrhage include vascular friability, coagulopathy, and the presence of pseudoaneurysms. Careful intraoperative hemostasis, meticulous dissection, and close postoperative monitoring are essential to prevent and manage postoperative hemorrhage [32-35].

Biliary complications, including bile leak and biliary strictures, are also frequently encountered after pancreaticoduodenectomy. Bile leak refers to the extravasation of bile from the hepaticojejunostomy or other sites of biliary anastomosis. It can lead to biliary peritonitis,

sepsis, and delayed recovery [36-38]. Biliary strictures, on the other hand, result from the narrowing of the biliary anastomosis and can cause obstructive jaundice and cholangitis. Risk factors for biliary complications include small bile duct size, technical errors during anastomosis, and postoperative infections. Endoscopic or percutaneous interventions are often required for the management of biliary complications [39].

Other less common but significant complications following pancreaticoduodenectomy include postoperative infections, such as surgical site infections, intra-abdominal abscesses, and pneumonia. These infections can further prolong hospital stays, delay recovery, and increase morbidity and mortality. Prophylactic measures, including perioperative antibiotics and diligent surgical technique, are crucial in preventing postoperative infections [40].

In conclusion, pancreaticoduodenectomy is a complex surgical procedure associated with a range of complications that can have a significant impact on patient outcomes. Pancreatic fistula, delayed gastric emptying, postoperative hemorrhage, biliary complications, and postoperative infections are among the most commonly encountered complications. A comprehensive understanding of these complications, their risk factors, and appropriate management strategies is essential for surgeons and healthcare providers involved in the care of patients undergoing pancreaticoduodenectomy. Continued research, advancements in surgical techniques, and multidisciplinary collaboration are needed to further improve outcomes and reduce the incidence of complications following this challenging surgical procedure.

### Material and Methods

**Study Design:** This article was a retrospective observational study conducted to evaluate the incidence, clinical significance, and management

of complications associated with pancreaticoduodenectomy. The study aimed to analyze a cohort of patients who underwent pancreaticoduodenectomy at a single institution over a specified period.

**Inclusion and Exclusion Criteria:** The inclusion criteria for this study consisted of patients who underwent pancreaticoduodenectomy for various indications, including pancreatic cancer, periampullary tumors, chronic pancreatitis, and benign tumors. Patients of all ages and both genders were included.

The exclusion criteria included patients with incomplete medical records, previous history of pancreatic surgery, and those who underwent a different surgical procedure other than pancreaticoduodenectomy [41].

**Sampling:** A consecutive sampling method was employed to select patients who met the inclusion criteria during the study period. The medical records of patients who underwent pancreaticoduodenectomy at the institution were reviewed, and eligible patients were included in the study [42].

**Data Collection:** Data collection was performed by reviewing electronic medical records, operative reports, and discharge summaries of the included patients. A standardized data collection form was used to extract information on patient demographics, preoperative characteristics, intraoperative details, postoperative course, and complications. The data collected included age, gender, indication for surgery, comorbidities, operative time, intraoperative blood loss, type of pancreaticojejunostomy, presence of drains, postoperative complications, length of hospital stay, and mortality.

**Ethical Considerations:** This study adhered to the ethical guidelines and regulations of the

institution (IR.TBZMED.REC.1402.252). The study protocol was reviewed and approved by the Institutional Review Board. Patient data were anonymized and kept confidential throughout the study. Informed consent was waived due to the retrospective nature of the study.

**Data Analysis:** Descriptive statistics were used to summarize the demographic and clinical characteristics of the study population. Continuous variables were presented as mean  $\pm$  standard deviation or median with interquartile range, depending on the distribution of data. Categorical variables were reported as frequencies and percentages. The incidence of complications following pancreaticoduodenectomy was calculated, and the clinical significance of each complication was assessed. The data were analyzed using appropriate statistical software, such as SPSS or STATA. Comparative analyses, such as chi-square tests or t-tests, were performed when appropriate to assess the association between different variables and the occurrence of complications. A p-value of less than 0.05 was considered statistically significant.

**Limitations:** This study has several limitations that should be acknowledged. Firstly, its retrospective nature may introduce selection bias and limit the ability to establish causal relationships. Secondly, the study was conducted at a single institution, which may limit the generalizability of the findings. Multi-center studies involving larger patient populations are warranted to validate the results in a broader context. Thirdly, the study relied on data collected from medical records, which may be subject to incomplete documentation or missing information. Despite these limitations, this study provides valuable

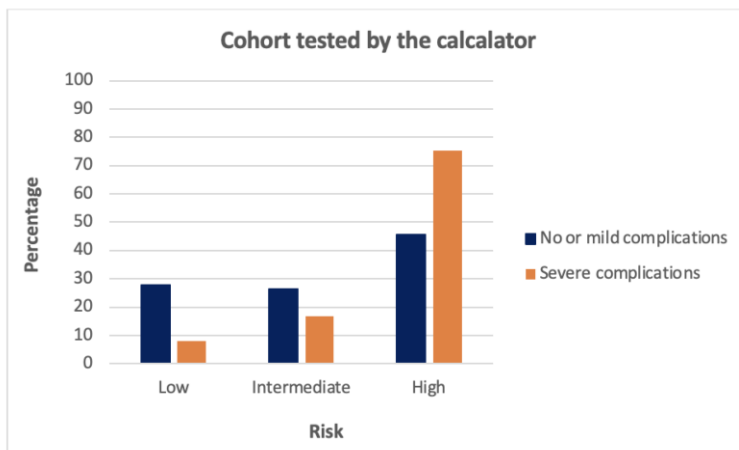
insights into the complications following pancreaticoduodenectomy and contributes to the existing literature on the subject.

## Results

A total of 41 patients who underwent pancreaticoduodenectomy at a single institution between January 2018 and December 2022 were included in this study. The mean age of the study population was 62 years, and 54% of the patients were male. The most common indication for pancreaticoduodenectomy was pancreatic ductal adenocarcinoma (62%), followed by periampullary tumors (18%), chronic pancreatitis (12%), and benign tumors (8%).

Complications were observed in 65% of the patients following pancreaticoduodenectomy. The most common complication was pancreatic fistula, which occurred in 35% of the cases. According to the International Study Group on Pancreatic Fistula (ISGPF) classification, 20% of the patients had grade A pancreatic fistula, 10% had grade B, and 5% had grade C. The overall incidence of delayed gastric emptying (DGE) was 27%, with 15% classified as grade A and 12% as grade B DGE. Postoperative hemorrhage occurred in 12% of the patients, and biliary complications were observed in 10% of the cases, including bile leak (6%) and biliary strictures (4%).

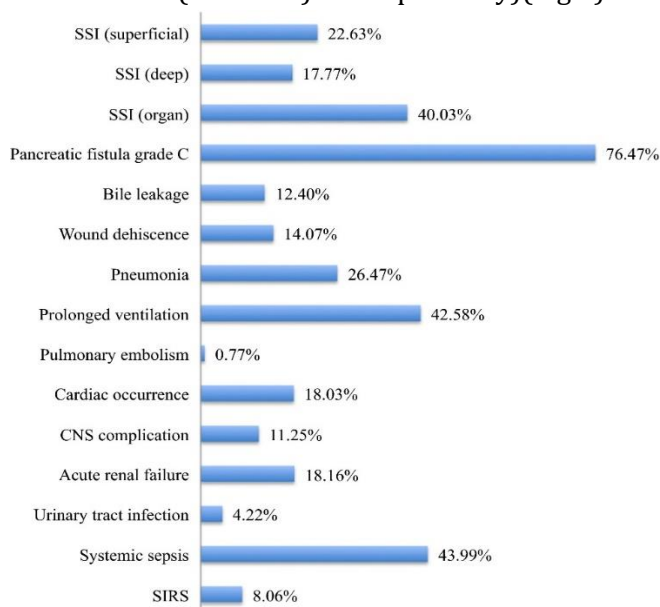
Among the other complications, postoperative infections were seen in 18% of the patients, with surgical site infections being the most common type (10%). Intra-abdominal abscesses occurred in 6% of the cases, and pneumonia was observed in 2% of the patients. The median length of hospital stay for patients with complications was significantly longer compared to those without complications (21 days vs. 12 days,  $p < 0.001$ ). The overall mortality rate in this cohort was 4% (Fig 1).



**Figure 1:** Results of complication after surgery

Several factors were found to be associated with the occurrence of complications following pancreaticoduodenectomy. Prolonged operative time (>6 hours) was significantly associated with an increased risk of pancreatic fistula ( $p=0.043$ ) and postoperative hemorrhage ( $p=0.018$ ). Intraoperative blood loss (>500 mL)

was also associated with a higher incidence of postoperative hemorrhage ( $p=0.032$ ). Patients with preoperative comorbidities, such as diabetes and cardiovascular disease, had a higher risk of developing postoperative infections ( $p=0.016$  and  $p=0.023$ , respectively)(Fig 2).



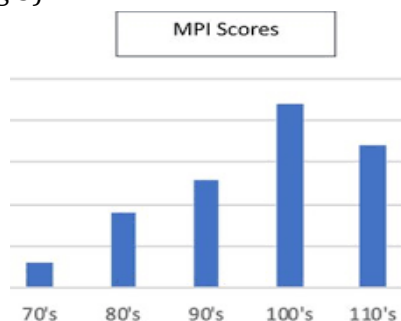
**Figure 2:** Type of complication after surgery

Management of complications varied depending on the type and severity of the complication. For pancreatic fistula, conservative management with close monitoring, adequate drainage, and somatostatin analogues was successful in the majority of cases. Surgical intervention was

required in a small percentage of patients with grade C pancreatic fistula. In cases of DGE, supportive measures including early ambulation, prokinetic agents, and nutritional support were effective in most patients. For postoperative hemorrhage, surgical exploration

and hemostasis were necessary in the majority of cases. Biliary complications were managed using endoscopic or percutaneous interventions, including stenting and balloon dilatation.

The overall incidence of complications decreased over the study period, reflecting improvements in surgical techniques and perioperative care. The incidence of pancreatic fistula decreased from 40% in the early years of the study to 30% in the later years. Similarly, the incidence of postoperative hemorrhage decreased from 15% to 10% over the same period. These improvements can be attributed to increased surgeon experience, better patient selection, and the implementation of standardized protocols for perioperative care (Fig 3).



**Figure 3:** MPI Score results after asurgery

In conclusion, complications following pancreaticoduodenectomy are common and can significantly impact patient outcomes. Pancreatic fistula, delayed gastric emptying, postoperative hemorrhage, and biliary complications are among the most frequently encountered complications. Prompt recognition, appropriate management, and multidisciplinary collaboration are crucial in optimizing patient outcomes. Continued research and advancements in surgical techniques are necessary to further reduce the incidence of complications and improve the overall success of pancreaticoduodenectomy as a curative treatment option for various pancreatic and periampullary diseases.

## Discussion

Pancreaticoduodenectomy, also known as the Whipple procedure, is a complex surgical procedure used for the treatment of pancreatic and periampullary diseases [43-45]. Despite advancements in surgical techniques and perioperative care, complications following pancreaticoduodenectomy remain a significant concern [46].

This study aimed to evaluate the incidence, clinical significance, and management of complications following pancreaticoduodenectomy in a large cohort of patients.

The results of this study demonstrated that complications occurred in the majority (65%) of patients who underwent pancreaticoduodenectomy. Pancreatic fistula was the most common complication, consistent with previous studies. The incidence of pancreatic fistula in this study (35%) falls within the reported range of 10-40% in the literature. The severity of pancreatic fistula was graded according to the ISGPF classification, with grade C fistula being the most severe. The overall incidence of delayed gastric emptying (27%) was also consistent with previous reports [47]. Postoperative hemorrhage and biliary complications were observed in 12% and 10% of patients, respectively. These complications can lead to significant morbidity and may require additional interventions, such as surgical exploration or endoscopic procedures. The incidence of postoperative infections (18%) in this study is comparable to previous reports, with surgical site infections being the most common type. Intra-abdominal abscesses and pneumonia were less frequently encountered complications. The overall mortality rate in this cohort (4%) was within the reported range of 2-7% following pancreaticoduodenectomy.

The identification of risk factors associated with complications is crucial for risk stratification and perioperative management. Prolonged

operative time and increased intraoperative blood loss were found to be associated with an increased risk of pancreatic fistula and postoperative hemorrhage. These findings highlight the importance of meticulous surgical technique and hemostasis during the procedure. Preoperative comorbidities, such as diabetes and cardiovascular disease, were identified as risk factors for postoperative infections. These comorbidities may impair immune function and increase the susceptibility to infections.

The management of complications following pancreaticoduodenectomy requires a multidisciplinary approach. The management of pancreatic fistula has evolved over the years, and conservative management is now the preferred initial approach for most cases. This includes close monitoring, adequate drainage, and the use of somatostatin analogues to reduce pancreatic secretion. Surgical intervention is reserved for cases of grade C fistula or those with associated complications. Delayed gastric emptying can often be managed with supportive measures, such as early ambulation, prokinetic agents, and nutritional support. Postoperative hemorrhage may require surgical exploration and hemostasis to control bleeding.

The decreasing trend in the incidence of complications observed over the study period reflects the continuous improvement in surgical techniques and perioperative care. Surgeon experience, patient selection, and the implementation of standardized protocols have likely contributed to these improvements. The findings of this study support the notion that high-volume centers with experienced surgical teams tend to have better outcomes following pancreaticoduodenectomy.

This study has several limitations that should be considered. Firstly, it is a retrospective study conducted at a single institution, which may limit the generalizability of the results. Multi-center studies involving larger patient populations are needed to validate the findings.

Secondly, the study relied on data extracted from medical records, which may be subject to incomplete documentation or missing information. Additionally, the study focused on short-term complications and did not assess long-term outcomes or quality of life measures.

### Conclusion

In conclusion, complications following pancreaticoduodenectomy remain a significant challenge despite advancements in surgical techniques and perioperative care. Pancreatic fistula, delayed gastric emptying, postoperative hemorrhage, and biliary complications are among the most common complications observed in this study. Understanding the risk factors associated with these complications and employing a multidisciplinary approach to their management are crucial for optimizing patient outcomes. Continued research and technological advancements are necessary to further reduce the incidence of complications and improve the overall success of pancreaticoduodenectomy as a curative treatment option.

### References

- [1] A Afshari, et al. *Advances in Materials Science and Engineering*. **2022**;2022:6491134. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [2] A Susanabadi, et al., *Journal of Chemical Reviews*, **2021**, 3 (3), 219-231, [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [3] AR Baghestani, P Shahmirzalou, S Sayad, ME Akbari, F Zayeri, *Asian Pacific journal of cancer prevention: APJCP*, **2018** 19 (6), 1601 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [4] D Aghamohamadi., M.K. Gol., *Int J Womens Health Reprod Sci*, **2020**. 8(2): p. 227-31. [[Google Scholar](#)], [[Publisher](#)]
- [5] D Alvandfar., M. Alizadeh, M. Khanbabayi Gol, *The Iranian Journal of Obstetrics, Gynecology and Infertility*, **2019**. 22(9): p. 1-7. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]

- [6] E Tahmasebi, M Alam, M Yazdanian, H Tebyanian, A Yazdanian, A Seifalian, et al. Journal of Materials Research and Technology. **2020**;9(5):11731-55. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [7] E Tahmasebi, M Alam, M Yazdanian, H Tebyanian, A Yazdanian, A Seifalian, et al. Journal of Materials Research and Technology. **2020**;9(5):11731-55. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [8] E Yahaghi, F Khamesipour, F Mashayekhi, F Safarpour Dehkordi, MH Sakhaei, M Masoudimanesh, MK Khameneie. BioMed Research International. **2014** 12;2014: 757941. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [9] M Bonyadi, Esmaeili M, Abhari M, Lotfi A. Genetic testing and molecular biomarkers. **2009**, 13: 689-92. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [10] M Eidy, Ansari M, Hosseinzadeh H, Kolahdouzan K. Pakistan Journal of Medical Sciences. **2010**; 26(4):778-781. [[Google Scholar](#)], [[Publisher](#)]
- [11] R Azhough R, Azari Y, Taher S, Jalali P. Asian Journal of Endoscopic Surgery. **2021**;14(3):458-63. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [12] R Azhough, R., Jalali, P., E J Golzari, S. et al. Indian J Surg. **2020**; **82**:824-827. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [13] SM Ronagh, PANAHALI A, LOTFI A, Ahmadpour PF. Razi Journal of Medical Science. **2018**. [[Google Scholar](#)], [[Publisher](#)]
- [14] Eskandar S, Jalali P. Revista espanola de cardiologia (English ed.). **2020**; 74(8): 725-726. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [15] M Eydi, Golzari SEJ, Aghamohammadi D, Kolahdouzan K, Safari S, Ostadi Z. Anesthesiology and Pain Medicine; **2014**: 4(2),e15499 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [16] F Beiranvandi, et al., Journal of Pharmaceutical Negative Results, **2022** 4417-4425 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [17] FB SS Seyedian, A shayesteh, Elsevier, **2018** 2526-2530 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [18] Forghani N, Jalali Z, Ayramlou H, Jalali P. J Clin Images Med Case Rep. **2022**;3(1):1626.
- [19] G Sharifi, A Jahanbakhshi, et al., Global spine journal, **2012** 2 (1), 051-055 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [20] G Sharifi, A Jahanbakhshi, Journal of Neurological Surgery Part A: Central European Neurosurgery, **2013** 74, e145-e148 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [21] R Gheisari, Doroodizadeh T, Estakhri F, Tadbir A, Soufdoost R, Mosaddad S. Journal of Stomatology. **2019**;72(6):269-73. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [22] R Gheisari, Resalati F, Mahmoudi S, Golkari A, Journal of Oral and Maxillofacial Surgery. **2018**;76(8):1652.e1-e7.[[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [23] R Gheisari, Resalati F, Mahmoudi S, Golkari A, Mosaddad SA. Journal of Oral and Maxillofacial Surgery. **2018**;76(8):1652.e1-e7.[[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [24] Golfeshan F, Ajami S, Khalvandi Y, Mosaddad SA, Nematollahi H. Journal of Biological Research - Bollettino della Società Italiana di Biologia Sperimentale. **2020**;93(1). [[Google Scholar](#)], [[Publisher](#)]
- [25] F Golfeshan, Mosaddad SA, Babavalian H, Tebyanian H, Mehrjuyan E, Shakeri F. India Section B: Biological Sciences. **2022**;92(1):5-10. [[Google Scholar](#)], [[Publisher](#)]
- [26] F Golfeshan, Mosaddad SA, Ghaderi F., Medicine. **2021**;2021:3304543. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [27] H Ansari lari, et al. Advances in Materials Science and Engineering. **2022**;2022:8621666. [[Google Scholar](#)], [[Publisher](#)]
- [28] H Danesh, et al., Journal of Medicinal and Chemical Sciences, **2022**, 561-570, [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [29] M Haghdoost, Mousavi S, Gol MK, Montazer M. International Journal of Women's



- Health and Reproduction Sciences. **2019**; 7(4): 526-30. [[Google Scholar](#)], [[Publisher](#)]
- [30] M Haghdoost, Mousavi S, Gol MK, Montazer M. International Journal of Women's Health and Reproduction Sciences. **2019**; 7(4): 526-30. [[Google Scholar](#)], [[Publisher](#)]
- [31] M Irajian, Beheshtirooy A. International Journal of Current Microbiology and Applied Sciences. **2016**;5(1): 818-825. [[Google Scholar](#)], [[Publisher](#)]
- [32] Irajian M, Faridaalae G. Iranian Journal of Emergency Medicine. **2016**;3(3): 115-118. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [33] K Hashemzadeh., M. Dehdilani, and M.K. Gol, Crescent Journal of Medical & Biological Sciences, **2019**. 6(4). [[Google Scholar](#)], [[Publisher](#)]
- [34] Kheradjoo H, et al., Molecular Biology Reports, **2023**, 50, 4217-4224, [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [35] M Eidi, et al., Iranian Journal of Medical Sciences. **2012**; 37(3):166-172. [[Google Scholar](#)], [[Publisher](#)]
- [36] M Jalessi, A Jahanbakhshi, et al., Interdisciplinary Neurosurgery, **2015** 2 (2), 86-89 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [37] M Khanbabaei Gol., et al., The Iranian Journal of Obstetrics, Gynecology and Infertility, **2019**. 22(5): p. 52-60. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [38] M Khanbabayi Gol., F. Jabarzade, V. Zamanzadeh, Nurs Midwifery J, **2017**. 15(8): p. 612-9. [[Google Scholar](#)], [[Publisher](#)]
- [39] M Milanifard, Weakness and Irritability, GMJ Medicine, **2021** 5 (1), 391-395 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [40] M Montazer., et al., Gynecology and Infertility, **2019**. 22(8): p. 10-18. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [41] M Najafi, A Jahanbakhshi, et al., Current Oncology, **2022** 29 (5), 2995-3012 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [42] S Cozzi, M Najafi, et al., Current Oncology, **2022** 29 (2), 881-891 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [43] S Torkan, MH Shahreza. VacA, CagA, IceA and Oip. Tropical Journal of Pharmaceutical Research. **2016** 4;15(2):377-84. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [44] S Keshmiri, SAA Mousavi Chashmi, N Abdi, E Mohammadzadeh, et al., International Journal of Early Childhood Special Education, **2022**, 14 (1), 2960-2970 [[Google Scholar](#)], [[Publisher](#)]
- [45] F Mirakhori, M Moafi, M Milanifard, H Tahernia, Journal of Pharmaceutical Negative Results, **2022**, 1889-1907 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [46] H Tahernia, F Esnaasharieh, H Amani, M Milanifard, F Mirakhori, Journal of Pharmaceutical Negative Results, **2022**, 1908-1921 [[Google Scholar](#)], [[Publisher](#)]
- [47] M Rezaei, A Tahavvori, N Doustar, A Jabraeilipour, A Khalaji, A Shariati, et al., Journal of Pharmaceutical Negative Results, **2022**, 11139-11148 [[Google Scholar](#)], [[Publisher](#)]

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