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PERSPECTIVE

Human–Pig Chimeric Organ in Organ Transplantation from Islamic Bioethics Perspectives

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Abstract

The use of pig derivatives in medicine is forbidden in Islamic law texts, despite the fact that certain applications offer medical advantages. Pigs can be one of the best human organ hosts; therefore, using human–pig chimeras may generate beneficial impact in organ transplantation, particularly in xenotransplantation. In Islam, medical emergencies may allow some pig-based treatments and medical procedures to be employed therapeutically. However, depending on the sort of medical use, emergency situation might differ. Using Islamic legal maxim as bioethical framework, the purpose of this study is to examine the use of pigs for the purpose of human–pig chimeric transplant from the perspective of Islamic bioethics. According to the findings, chimeric organ transplantation using pigs should only be done in emergency situations.

Keywords Chimera · Organ transplantation · Transplant ethics · Islamic legal maxim · Human–pig organ

Introduction

Pigs are the best hosts for human organs in chimeric organ transplantation due to their organ size similarities, simplicity of genetic editing, and short reproductive time (Loike and Kadish 2018; Zhong et al. 2019). On the other hand, pigs are prohibited from consumption and use for Muslims, as stated in Quranic verses and Sunnah, since they are classified as *najs mughallazah* or severely impure (Al-Zuhaili 2010). Chapter al-Baqarah, verse 173, recorded a ban on consuming pig

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and its derivatives: "He has only forbidden you carrion, blood, pig's meat, and animals over which any name other than God's has been invoked. But if anyone is forced to eat such things by hunger, rather than desire or excess, he commits no sin: God is most merciful and forgiving" (al-Baqarah: 173). The same prohibition is also recorded in Chapter al-Maidah, verse 3, and Chapter al-Nahl, verse 115.

The above verse clearly indicates the prohibition on the consumption of pigs. Muslim scholars also associate lard in the ban (Al-Qurtubi 2006; At-Tabari 1994; Ibn Kathir 1999). This prohibition is also supported by the Sunnah of the Prophet narrated by Jabir bin Abdillah, when he heard the Prophet say, "Allah and His Apostle made illegal trade of alcohol, dead animals, pigs and idols" (Al-Bukhari 2002). The ban on trading pigs is due to their impurity (Hajar 2008). Furthermore, excrement is a substance that cannot be used as medicine as narrated by al-Tirmidhi (At-Tirmidzi 1996). Al-Zuhaili added that the Muslim scholars agreed that the impurity of the pig includes meat, bones, blood, fat, fur, and skin even if slaughtered in a lawful (halal) way (Al-Zuhaili 2010). As a result, all medical treatments using pigs or their derivatives are prohibited, including the transplantation of human–pig chimeric organs, as contamination with pig derivatives is expected especially from the pig tissues in the organ. Chimeric organs are created from human stem cells and implanted into host animals such as pigs and monkeys (Wu et al. 2017; Tan et al. 2021). Therefore, this paper will examine the Islamic bioethics perspective on the use of mixed organs made up of human and pig cells for organ transplantation to help patients who need new organs.

Human–Animal Chimera

Chimera organs are created for organ transplantation. Human–animal chimera research began in 1969, intended to study human biology (Rygaard and Povlsen 1969). However, in 2017, pigs began to be served as a host for human organs to create human–pig chimeras that can be an alternative source of organs for organ transplantation (Wu et al. 2017). Chimera organs are produced via blastocyst complementation. This procedure has been successfully used to create chimeras between mammalian species by Kobayashi, in which earlier, he successfully created a rat's pancreas in a mouse using rat stem cells (Kobayashi et al. 2010). On the other hand, human–animal chimeras are created through the injection of patient stem cells into host animal blastocytes (Lu et al. 2019). A chimeric organ can be transplanted to a patient with little to no need for immunosuppressive medications, which lowers the cost of therapy and is more beneficial and significant to be an alternative source of organs (Loike and Kadish 2018). This situation, however, can only be accomplished if the organs created have a majority of patient cells. However, on the other hand, if not adequately regulated, chimeric organ transplantation might have adverse effects such as virus transmission, tumor growth, and immune rejection due to contamination of animal cells (Lu et al. 2019; Loike and Kadish 2018). In April 2021, Jun Wu's work successfully

created a human–monkey chimera for 20 days until it had to be destroyed due to ethical restrictions. The study was conducted in hope to alleviate the shortage of donated organs for transplantation treatment (Tan et al. 2021).

The Islamic Ethical Concerns on Human–Animal Chimera

From an Islamic perspective, there has been no clear debate to date on the production of human–animal chimeric organs. The debate closest to the human–animal chimera is the debate on the transfer of stem cells into animals, issued in a medical fatwa by Dar al-Ifta Misriyyah. The fatwa issued by the institution allows research on human stem cells on animals to benefit humans based on the Quranic verses stating that humans can use animals to gain benefit (Dar-Alifta Al-Misriyyah 2008). The term used in the Quran was *taskhir*, which is not limited to "use" only, but also include consumption and any activities that may benefit human. However, the production of human organs in animals can raise issues requiring in-depth studies because when human stem cells spread to the animal's brain or gametes intentionally or unintentionally, it will cause the humanization of animals and raise various bioethical issues (Suchy and Nakauchi 2018).

Human–animal chimera creation or the act of fusing human and animal cells to create chimeric organs is considered altering with God's creation (*taghyir khalqil-lah*). "(Satan said) "and I will lead them astray, and I will tempt them with false hopes, and I will command them, whereby they shall slit the ears of cattle, and I will command them, whereby they shall alter the creation of Allah." Whoever takes Satan for a friend, instead of Allah, incurs an obvious loss," says verse 119 of the Chapter al-Nisa'. Through this verse, many definitions on altering the creation of Allah have been given by the scholars, but Hamdan et al. have concluded that altering God's creation alters God's religion, castration, tattooing, altering God's law, and associating God with other things (Hamdan and Ramli, 2018; Hamdan et al. 2021). Al-Qurtubi added according to the majority of Muslim scholars, castration of people is prohibited, while castration of cattle is permitted for their benefit (Al-Qurtubi 2006). Ibn Attiyah also added physical change is acceptable if it is beneficial, but it is not permissible if it is harmful (Ibn Attiyah 2001). Thus, a strong justification is needed if one wants to use altered animals in medicine.

Besides, human dignity is also tarnished by the formation of chimeras that humanize animals. Allah honored humans more than animals in Chapter al-Isra' verse 70 where He stated, "We have honoured the children of Adam and carried them by land and sea; We have provided good substance for them and favoured them specially above many of those We have created." Animals can be humanized in terms of their exterior appearance as well as their neurological systems to have human features. The human–animal chimera development experiment's main issue is that the humanization of the neurological system might lead to moral confusion between humans and nonhumans, as well as a degradation of human dignity. Neurological humanization can result when human cells are implanted into an animal's embryo that is later fertilized or into an animal's brain system (Hyun 2018). Human cells will invade the animal's brain and change the structure of the

animal's brain (Windrem et al. 2014). When this happens, the animal will become smarter as demonstrated by Windrem et al. (2014) and Goldman et al. (2016) in their studies where human cells dominated the brain of nude mice and made them smarter than other mice in terms of learning tasks.

The verse in Chapter al-Isra' explained that humans are honored because they are endowed with intelligence that carries the commandments (*taklif*), and with it, humans may learn about Allah and His instructions, leading to His bliss and obedience to His Messengers. Meanwhile, the phrase "favoured them specially above many of those We have created" indicates that humans are superior to cattle, animals, beasts, and birds (Al-Qurtubi 2006). This suggests that God bestowed intelligence on humans as a mark of distinction between humans and animals. Thus, humanizing animal neurology by giving animals human-like intellect may result in the degradation of human dignity.

Furthermore, if human–animal chimeric organs are utilized as organ sources for organ transplantation, the virus has the potential to propagate. Some animals used as hosts for human cells in experiment have been found as virus carriers, such as crab-eating monkeys that have been confirmed to carry the herpes-B virus and pigs that have been shown to contain swine influenza viruses such as H1N1 (Ostrowski et al. 1998; WHO 2018). The ethics committees are mainly concerned about viral transmission in this form of organ transplant since most infectious illnesses, such as the bubonic plague, the flu, and HIV, are caused by viruses that are transmitted to humans from animals. These infectious illnesses, including the SARS virus passed from civet to human, are the source of the pandemic (Huther 2009). In addition to stringent control, the best choice is to pick animal species that have not been confirmed to be viral carriers. The misconduct of the animal chosen as the host is likely to become a carrier of the virus and spread it. Therefore, it violates the objectives of Sharia in medicine which is to preserve life because medicine should fulfill the objectives of Sharia especially in protecting life.

Lastly, the purity status of organs that combine human and animal cells, such as pigs, remains unclear. It has previously been declared that medicating using excrete-containing compounds is prohibited. The Prophet Muhammad PBUH said that any part of the animal that is removed while it is still alive is a filthy product and categorized it as a carcass (Al-Zuhaili 2010). As a result, the chimeric organ recovered from live animals can be categorized as carcass and included in this prohibition.

Islamic Legal Maxims on Human–Pig Organ Transplantation

Islamic legal maxims established that the emergency or necessity situation, known as *darurah*, may allow several prohibited things to become acceptable. This legal maxim states that an emergency crisis or desperation may permit a person to commit acts prohibited by Sharia law (Syibir 2014). It comes from the same verse after the banning of pigs in the same Chapter al-Baqarah, verse 173. As a result, the question arises whether the use of human organs grown in pig

bodies to save the lives of people in need of replacement organs also falls under this law. Emergency situations are frequently referred to dangerous situations or those resulting in death. Al-Raisuni (2008) emphasized that when a person reaches a point of extreme difficulty or danger, he or she must discover a route out to avoid remaining in the position (Al-Raisuni 2008). Pigs are frequently used in medical procedures such as vaccine development, insulin manufacture, and even xenotransplantation. However, all medical interventions must adhere to the Islamic legal maxim, which states the following: (1) such difficulties must be unexpected and clearly jeopardize one of Islamic five primary objectives, known as *daruriyyat al-khams*, which is to preserve religion, life, property, dignity, and intellect; (2) there is no other lawful way to eliminate such inconvenience; and (3) the use of prohibited resources must be limited solely to alleviate the inconvenience (Syibir 2014).

Al-Azhar has released a statement regarding the xenotransplantation of pig kidneys. According to them, xenotransplantation of swine kidneys to humans is not permitted unless an emergency situation and the following two conditions are met: the swine organs are merely a substitute for fatal organs, and the risk for continuing the transplantation is lesser than not continuing it. This is consistent with two Islamic legal maxims: (i) *al-darar yuzal* (difficulties must be eliminated) and (ii) *'idha ta'radat mafsadatan ru'iy 'azamuhuma dhararan bi irtikab 'akhaffuhima* (if two difficulties collide, great difficulties must be eliminated by doing the lightest) (Hassan 2021). The same legal maxim may be used with human–pig organs since organs blended with human and pig tissue are also forbidden in Islam. However, this treatment can benefit humans.

An emergency situation occurs when there is an absence of a suitable human organ host from lawful animal, and the necessity to create organs in an unlawful (haram) animal host such as pig is considered a preferable option. The choice of treatment procedure must be with the aim of curing the patient without more severe risk based on the Islamic legal maxim, which enjoins avoiding harm. One way to create chimeric organ is to use pigs as the host animal for human organ. However, the use of pigs as hosts is clearly prohibited in the Islamic ruling. In addition to pigs, primate species are also able to act as suitable hosts for humans because their physiology is very similar to humans (Shaw et al. 2014). Moreover, non-human primates and large livestock animals must only be used in research under the direct supervision of veterinary professionals and frequent monitoring whenever unexpected results and surprising phenotypes could happen (International Society for Stem Cell Research 2021). However, there is no denying the existence of more lawful animals such as cows, goats, and other livestock to be used as hosts of human organs. The primary factor is the suitability of organogenesis, which prevents these animals from being used as hosts for human organs. Similarly, in the case of xenotransplantation, the pig organ was chosen because of its suitability for humans, such as organ size (Loike and Kadish 2018). If lawful animals are suitable as a host for human organs, then the permissibility of using the unlawful animal as a host is revoked because it does not meet the requirements of using unlawful animals according to the Islamic legal maxim, which says, there is no other lawful way to eliminate such inconvenience.

If in a situation that requires a new functional organ, the patient is often given the option of receiving a halal allogenic organ transplant, which requires the patient to rely on immunosuppressants for the rest of his or her life to prevent the body's immune system from rejecting the organ (Black et al. 2018). In the absence of an appropriate allogenic organ, the patient is given the option of receiving a xenogeneic organ, which also requires the patient to rely on lifelong immunosuppressants. Therefore, one option is to receive an organ made with their own stem cells that do not require immunosuppressants, with the help of gene editing that edits the organ (Loike and Kadish 2018). Patients waiting to receive a suitable allogeneic organ may have to wait for months or longer (National Kidney Foundation n.d.). The same period is also likely to produce human–animal chimera organs. Furthermore, if the possibility of organ failure can be detected from the beginning, then preparations to produce human–animal organs can also be made earlier. Therefore, patients do not have to wait for a long period of time. Furthermore, if the waiting period for human–animal chimera organs and allogenic organs is more or less the same, then human–animal chimera organs are preferable because patients do not have to rely on other people's organs.

According to the situation, emergencies may also include the use of human organs grown in pig hosts as a supply of donor organs. Indeed, it is preferable if the chimeric organ is entirely composed of human cells and is free of pig cells. Additionally, body rejection, xenotransplantation-related adverse effects, and significant health issues should be considered to ensure that the medical intervention chosen is more beneficial than detrimental to the patient (Hassan 2021). Thus, the chimeric organ should contain at least 90% human or patient cells to minimize these adverse consequences (Loike and Kadish 2018). CRISPR or any other genetic editing technology also contributes to the reduction of side effects by genetically engineering host pigs to be virus- and symptom-free (Sykes and Sachs 2019). As a result, it can be argued that human–pig chimeric organ transplantation has the potential to be a viable option for treating organ injury and should be permitted in emergencies. Although this option is still in its early stages of development, it has demonstrated its potential as a safe therapeutic choice.

Conclusion

The use of pigs as hosts for human organs because of their suitability needs careful scrutiny from the context of Islam, especially when there is a ban on using pigs or pig derivatives even in medicine. Furthermore, there are several other issues that are prohibited in Islam when human organs are produced in pigs such as disgusted feeling among Muslim when involving pig and animal welfare. However, this ban can be lifted in an emergency situation. After examining the application of Islamic legal maxims pertaining to the use of human–pig chimera for organ transplantation, it can be concluded that the use of human–pig chimera should be allowed only in an emergency situation.

Author Contribution Muhammad Faiq Mohd Zailani and Mohammad Naqib Hamdan conceived the presented idea. Data collection and data analysis were performed by Muhammad Faiq Mohd Zailani under the supervision of Mohammad Naqib Hamdan and Aimi Nadia Mohd Yusof. The first draft of the manuscript was written by Muhammad Faiq Mohd Zailani and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Declarations

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Consent to Participate Not applicable.

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